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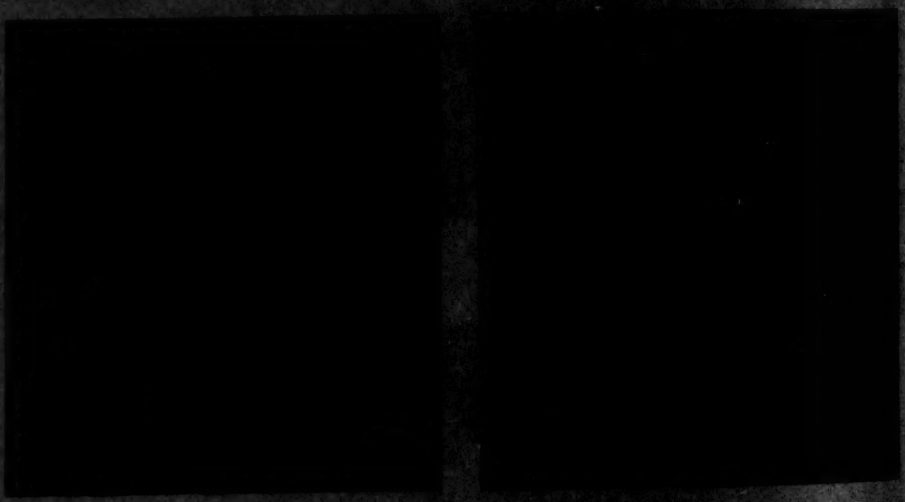

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OPHTHALMOLOGY

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COMMUNICATIONS

STUDIES ON THE INTRA-OCULAR FLUIDS

2.—The Penetration of Certain Ions into the Aqueous Humour and Vitreous Body*

BY

SIR STEWART DUKE-ELDER, H. DAVSON

and D. M. MAURICE

From the Ophthalmological Research Unit, Medical Research Council. The Institute of Ophthalmology, London

IN the first of this series of papers (Duke-Elder and Davson, 1949) a detailed study was made of the entry of sugars into the various parts of the eye from the blood; the present paper is a continuation of the same study with regard to salts. Exchanges of water between the blood and intra-ocular fluids occur rapidly, so rapidly as to indicate that these exchanges take place over a wide area of contact between the two systems and are not confined to a limited region such as the ciliary body. The osmosis of water into, or out of, the eye must influence the intra-ocular pressure immediately and effectively; and, since it is the salt content of the two fluids that

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largely determines their osmotic pressures, the conditions under which salts may penetrate from the blood into the intra-ocular fluids are of fundamental importance. It has been shown from this laboratory that the osmotic pressure of the aqueous humour is greater than that of plasma (Benham, Duke-Elder and Hodgson, 1937) and again that the difference in osmotic pressure is due, at least in part, to an excess of sodium and chloride ions in the aqueous humour over that demanded by the Donnan equilibrium (Davson, Duke-Elder and Maurice, 1948). On these grounds, therefore, we may expect that sodium and chloride will be secreted into the eye, but whether or not the only mode of entry of these and other ions is by a secretory process from the ciliary epithelium is a matter that has not yet been decided.

THEORETICAL

It is hoped that kinetic studies on the mode of penetration of certain ions will throw some light on the problem, although in view of the formal similarity of certain equations for diffusion to those for secretion, it seems unlikely that a mere mathematical analysis of the process of penetration of a given ion can decide whether it is entering by a simple process of diffusion or secretion, or by a combination of these. The development of the mathematical formulae required here has been taken up elsewhere (Davson, Duke-Elder, Maurice, Ross and Woodin, 1949); for our purpose we need only indicate that the rate of penetration of a substance into the aqueous humour may be presented in the form of a parameter, K'_A, calculated from the experimental material by substitution in the following formula:—

$$\frac{r}{t} \log \frac{rC_p - C_{Aqo}}{rC_p - C_{Aq}} = K'$$

where t is the time of penetration in hours, C_p and C_{Aq} are the concentrations of the substance in plasma and aqueous humour at time t; C_{Aqo} is the original concentration in the aqueous humour and r is the ratio $\frac{C_{Aq}}{C_p}$ at infinite time. A parameter, K'_V, for penetration into the vitreous body, is computed similarly from the appropriate concentrations in this fluid.

The principal assumption at the basis of the derivation of the formula is that the penetration occurs in accordance with Fick's Law, *i.e.*, that the rate of transfer across the blood-aqueous barrier is proportional to the concentration gradient across the barrier.

METHODS

General. The operative technique was similar in essentials to that described earlier (Duke-Elder and Davson, 1949); a high and relatively constant concentration of a given substance was maintained in the blood of a cat anaesthetised with nembutal. This was achieved, in general, by a single intravenous injection of an isotonic solution followed by repeated smaller injections in accordance with empirically determined schedules which varied with the substance considered. In the case of radio-active potassium (K^{42}), however, the rate of loss from the blood was so rapid that it was impracticable to maintain a constant high level; consequently the solution was injected by a drip-infusion technique. The concentration of K^{42} rose rapidly during the first few minutes, and then more slowly and approximately linearly during the rest of the experiment. K'_A and K'_V were calculated by graphical integration. The eyes and blood samples were removed at appropriate intervals and the aqueous humour, vitreous body and plasma submitted to analysis.

Chemical. Thiocyanate was determined by the colorimetric technique of Aldridge (1945) on trichloracetic acid filtrates.

Radio-active Tracers. With the exceptions described below, all the determinations of radio-active tracers were done with the pipette-type counter described earlier (Maurice, 1948) and figured and described in Fig. 1. It was supplied with its high tension from a Dynatron Type 200 power unit, the counts being recorded on a Type 200 scale-of-ten scaler preceded by a modified Neher-Pickering circuit. The counter was always washed and dried between samples except when there was a reasonable certainty that their difference in activity was small. Sufficient counts were made to give a standard deviation of between one and two per cent. in case of plasma and aqueous humour, and of five per cent. in case of the vitreous body,

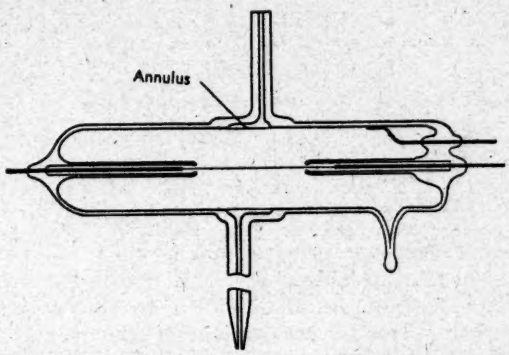

FIG. 1.

PIPETTE-TYPE GEIGER COUNTER FOR SMALL QUANTITIES OF BIOLOGICAL FLUIDS

The sample to be assayed (0·5 ml.) is sucked into the glass annulus which is formed round the cylindrical body of the counter itself and separated from it by a very thin glass wall. A high voltage is applied between the central wire and the wall of the counter, which is then sensitive to radio-active particles passing into it from the sample. These are individually registered on auxiliary apparatus. The number of particles counted in a given time is proportional to the concentration of the radio-active material in the sample.

Corrections were applied for the background count, the radio-active decay of the samples, and the resolution time of the counter. This last correction never rose above two or three per cent. The counter-voltage and the temperature were noted but they never varied sufficiently during an experiment to make a correction necessary.

In the case of the first five measurements of Na^{24} activity, the samples were measured into small glass dishes, which were stood on the window of a bell-type counter and located by means of a wax cast fixed by the edge of the window. Quadruplicate 0·2 ml. samples were used, the agreement being that expected from the number of counts taken.

For the first four phosphate determinations the sample, after removal of proteins if necessary, was treated with sufficient sodium phosphate solution to give about 1 mg. of precipitate, excess of magnesium and ammonium chlorides was added and the mixture made alkaline with ammonia. The precipitate of magnesium ammonium phosphate was collected by suction on a sintered glass filter, 4 mm. in diameter, sealed into the end of a glass tube. It was found necessary to repeat the precipitation on the first filtrate in order to complete the collection of the phosphate. The collected precipitate was dried and the "filter stick" was accurately positioned by a brass frame in proximity with the window of a bell-type counter.

Na^{24} was used in the form of sodium chloride with an activity of 1 mC per g.; K^{42} as potassium chloride of similar activity. P^{32} was received as a solution of phosphoric acid containing less than 10 mg. per ml. of total solids and with an activity greater than 0.3 mC per ml. and this was brought to pH 7·4 with NaOH.

TABLE I

THE RELATIVE RATES OF PENETRATION OF CERTAIN IONS INTO THE INTRA-OCULAR FLUIDS

Substance	No. of Expts.	100 K'_A	100 K'_V	K'_A/K'_V
Thiocyanate	12	46·5 ± 2·3	18·3 ± 1	2·5
Sodium	15	37·6 ± 1·2	6·8 ± 0·3	5·5
Potassium	14	42 — 31	12 — 7·7	3·5 — 4
Phosphate	6	5·2 ± 0·9	0·33 ± 0·05	16

RESULTS

The *relative rates of penetration* of thiocyanate, sodium, potassium and phosphate into the intra-ocular fluids are shown in Table I. The differences in the rates of penetration are of considerable significance. In the first place the rate of penetration of thiocyanate is significantly greater than that of either sodium or potassium; and all three of these ions penetrate very much more rapidly than phosphate. The slow rate of penetration of the latter substance agrees with the results of a more exhaustive study by Palm (1948) on the rabbit. That thiocyanate enters more rapidly than sodium was confirmed by injecting both radio-active sodium and thiocyanate into the same animal, and measuring the rates of penetration of both. The mean of two experiments gave the following:—

	K'_A	K'_V
Sodium	34.4	6.8
Thiocyanate	43.7	20.7

A comparison of the rate of entry of thiocyanate and the sugars is also of interest. In the earlier paper of this series it was shown that the value of K'_A for the monosaccharides is, on the average, 32·5 and that for K'_V 11·2; it appears, therefore, that thiocyanate penetrates rather more rapidly than the monosaccharides into the aqueous humour and nearly twice as rapidly into the vitreous body. This is confirmed by simultaneous measurements on the same animal as is seen in Table II.

TABLE II

THE SIMULTANEOUS PENETRATION OF SUGAR AND THIOCYANATE INTO THE EYE OF THE CAT

Animal	Substance	100 K'_A	100 K'_V
No. 1	Thiocyanate	42·5	16·8
	Galactose	26·7	6·5
No. 2	Thiocyanate	40	20
	Glucose	27·1	7·8
No. 3	Thiocyanate	27·5	16
	Galactose	21·2	4·6

The variability of the rate of entry of potassium is noteworthy. In Table I the values of K′ for potassium have been indicated as a range varying between 42 and 31 for the aqueous humour and 12 and 7·7 for the vitreous body. This variability was due, in general, to the fact that the value of K′ determined from the first half-hour of penetration, was consistently greater than that obtained from the second half-hour. There is thus an unmistakable tendency for the rate of penetration of potassium to slow down during the course of the experiment under the conditions employed in this work. This matter is under investigation and will not be discussed further at present: the difference between the constants derived from the first and second half-hours of penetration is brought out by the following:—

K'_{A_1}	K'_{A_2}	K'_{V_1}	K'_{V_2}
40.5	30.3	11.8	7.4

which may be contrasted with the following figures for sodium:—

K'_{A_1}	K'_{A_2}	K'_{V_1}	K'_{V_2}
38.7	37.3	6.8	6.6

The site of penetration. In earlier experiments on the penetration of sugars (Duke-Elder and Davson, 1949) it was concluded that these substances entered the cavity of the eye from all the surrounding vascularized tissues. It will be remembered that this conclusion was based on the separate analysis of different sections of the frozen vitreous body. A similar technique was followed here, the frozen vitreous body being separated into three parts by sections at right angles to the antero-posterior axis, the anterior portion closest to

the ciliary body, the posterior part farthest away. If diffusion from the blood into the vitreous body occurred not only from the ciliary body but also from the whole of the posterior segment of the globe, the middle section would have the lowest concentration of the penetrating substance owing to the unfavourable area-volume relationship pertaining in this region. If, on the other hand, diffusion occurred exclusively from the ciliary body, the posterior portion would have the lowest concentration. As with the sugars

TABLE III

RELATIVE CONCENTRATIONS OF THIOCYANATE IN THE THREE SECTIONS OF THE VITREOUS BODY AFTER THE CONCENTRATION IN THE BLOOD HAD BEEN MAINTAINED AT A HIGH VALUE FOR VARIOUS TIMES

Time (min.)	Aqueous Humour	Concentration		Posterior
		Anterior	Middle	
30	100	46	49	46
30	100	55	64	82.5
31	100	47	34	55
34	100	39	28	33
38	100	53	37	64
60	100	58	42	44
60	100	55	37	57
60	100	56	52	80
60	100	68	68	80

TABLE IV

RELATIVE CONCENTRATIONS OF Na^{24} IN THE THREE SECTIONS OF THE VITREOUS BODY AFTER THE CONCENTRATION IN THE BLOOD HAD BEEN MAINTAINED AT A HIGH VALUE FOR VARIOUS TIMES

Time (min.)	Aqueous Humour	Relative Concentrations		Posterior
		Anterior	Middle	
28	100	44	12	18
60	100	38	29	25
7	100	27	12	6
8	100	24	11	10

it was found that with thiocyanate the middle sections, on the average, had the lowest concentration at the end of a given period of diffusion: the concentrations in the aqueous humour and the different parts of the vitreous body are as shown in Table III. One may tentatively conclude from these results, that thiocyanate diffuses into the vitreous body from all the vascularized tissue surrounding it. With radio-active sodium and potassium, on the other hand, a significantly different picture of distribution in the frozen vitreous body was obtained as is shown in Tables IV and V.

TABLE V

RELATIVE CONCENTRATIONS OF K^{42} IN THE THREE SECTIONS OF THE VITREOUS BODY AFTER THE CONCENTRATION IN THE BLOOD HAD BEEN MAINTAINED AT A HIGH VALUE FOR VARIOUS TIMES

Time (min.)	Aqueous Humour	Relative Concentrations		Posterior
		Anterior	Middle	
30·5	100	43	20	14
31	100	54	20	13
31	100	92	41	16
31	100	49	39	18
38	100	53	23	20
59	100	64	44	23
58	100	71	31	13

From these tables it will be seen that, with both sodium and potassium, by far the highest concentration is that found in the most anterior segment of the vitreous body which is in closest proximity to the ciliary body. The region having the smallest concentration is the most posterior segment which is farthest away from the ciliary body. From these findings it is difficult to escape the conclusion that penetration of sodium and potassium into the posterior segment of the eye is predominantly from the ciliary region.

DISCUSSION

We wish to discuss at present three points relating to the facts described in this paper. First, we have the observation that thiocyanate penetrates from the blood into the aqueous humour and vitreous body more rapidly than either sodium or potassium;

the difference in rate is particularly evident in respect to penetration into the vitreous body. This difference seems to rule out the possibility that the main route of penetration of salts is by water-filled pores as it is throughout the body generally, that is, by way of the inter-cellular spaces of the capillaries and the lining membranes of the eye. If this simple mechanism were responsible, the relative rates of penetration of the different ions would correspond with their ionic mobilities, *i.e.*, the values for sodium, potassium, and thiocyanate should be as 44 is to 65 is to 56. We may therefore conclude, on this count, that the factors of cell membrane permeability (lipoid solubility, adsorbability, etc.) play an important part in determining penetration into the intra-ocular fluids from the blood. It follows that, so far as these substances are concerned, *transference from the blood into the chambers of the eye takes place through cell bodies and not inter-cellular spaces*, a conclusion which is in conformity with the fact that the salt content of the aqueous humour is greater than can be accounted for by a simple process of ultra-filtration.

Secondly we may note that the relative rates of penetration into the aqueous and vitreous differ very considerably between the various substances studied. All the salts studied enter the vitreous more slowly than the aqueous, but while thiocyanate enters the former most easily, phosphates do so only in very small quantities. Thus the ratio K_A/K_V for the thiocyanate ion is 2·5 whilst for sodium and potassium it is in the region of 5 and for phosphate it is 16. It seems probable that these differences depend on the differing sites of penetration of the respective ions. The evidence presented here indicates that thiocyanate penetrates throughout all the vascularized parts of the eye, *i.e.*, from the entire uveal, and presumably the retinal, circulations while sodium and potassium penetrate into the posterior segment of the eye through a restricted area only—the ciliary region. If this is the case it is obvious that the rate of accumulation of the first substance in the vitreous body should be greater, other things being equal, than that of the latter two. It may be recalled here that the monosaccharides, which also appear to penetrate into the vitreous body from all parts of the barrier, gave a ratio of K_A/K_V of 2·9 which is comparable with that for thiocyanate. In discussing this point earlier (Davson and Duke-Elder, 1948), it was pointed out that, if the barrier between blood and vitreous body were more selective than that between blood and aqueous humour, we should expect the ratio of K_A/K_V to become greater, the slower the rate of penetration of a substance; thus with the sugars the ratio was 2·2 for a pentose; 3·3 for hexoses, and 17 for sucrose. The high ratio reported here for phosphate, namely 16, is probably due chiefly to this factor; the amounts

penetrating the vitreous body were so small that it was not feasible to estimate the separate amounts in different parts of the vitreous body and so to find out whether penetration was confined to the ciliary region or not.

A final word will not be out of place on the bearing of these results on the problem of the formation of the intra-ocular fluid. Such mathematical treatment as the results have been given has been on the basis of the assumption that the amount of substance entering the fluid in unit time is proportional to the concentration gradient at that moment; in other words it has been assumed that the penetration is determined by the simple physico-chemical laws of diffusion. With the possible exception of potassium, the experimental results conformed with the equations in the sense that the parameter K′ appeared to be independent of the concentration gradient and the time of penetration. One might be inclined, on the basis of this finding, to suggest that penetration of the salts discussed is predominantly a matter of simple diffusion. Such a conclusion, however, would be unjustified; it is easy, as Kinsey and Grant (1942) have shown, to establish an equation on the basis of a supposed secretory mechanism, which has essentially the same form as the one employed here and derived without any assumptions of secretory activity. Kinsey and Grant concluded that salts entered the eye by a process of secretion largely as a result of this conformity of their results with their arbitrary secretion equation, but it is quite evident that in the present state of our knowledge an appeal to the results of mathematical analysis unsupported by other evidence is not yet warrantable, since the same equation may be derived on the basis of such entirely different postulates (*Bárány* and Davson, 1948). It would seem, however, that since the concentration of salts into the intra-ocular fluids is higher than can be accounted for by a process of simple ultra-filtration, some cellular activity (that is, a process of secretion) in their transference must be postulated.

SUMMARY

1. The salt content of the intra-ocular fluids is greater than can be accounted for by a process of simple ultra-filtration. Some cellular activity is therefore involved in the transference across the blood-aqueous barrier: a process of secretion must be postulated.

2. The various electrolytes tested (sodium, potassium, thiocyanate) penetrate across the blood-aqueous barrier at varying rates which cannot be accounted for by a simple diffusion through inter-cellular spaces, but only by penetration through cell bodies.

3. While some ions (thiocyanate) penetrate into the intra-ocular fluids throughout the whole of the blood-aqueous barrier, others

(sodium) enter the posterior segment of the cavity of the eye (in large measure, at any rate) by way of the ciliary body.

All the thiocyanate determinations described in this paper were carried out by Mr. A. M. Woodin.

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DISEASES OF THE EYE IN RELATION TO DENTAL SURGERY*

BY

J. H. DOGGART

LONDON

THE current fashion of labelling diseases " allergic " has to some extent diverted attention from focal sepsis. Nevertheless that controversy is still alive, and it would be safe to predict widely varying estimates if any twelve ophthalmologists were invited to answer the question : " What percentage of the ocular disease in your practice is due to unhealthy teeth ? " There are, of course, many other organs and tissues on which attention has been riveted by people seeking to explain inflammatory lesions of the eye. The vermiform appendix, the colon, the prostate gland, the skin and the tonsils have all been singled out for blame, and that list might be greatly extended.

In all the mass of literature dealing with ocular disease of supposedly dental origin, one feature has escaped comment, so far as I have been able to ascertain. I refer to the curious assumption that infective traffic between the teeth and the eyes must be one-way. When will some champion take up the cudgels on behalf of these much-maligned gomphoses? Such a man might begin by

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proclaiming his disbelief in dental iridocyclitis, and then, carrying the war into the enemy's camp, he would doubtless marshall statistics whereby ocular lesions could be indicted as a source of parodontal disease. The main weakness of this doctrine would be that it could hardly be carried to its logical end, because total extraction is so infinitely more drastic a policy when dealing with eyes than with teeth. No such objection, however, would arise if the blame were put upon the ocular adnexa, which consist of the eyelids and lacrimal apparatus. When once an observer had convinced himself that among the convolutions of the Meibomian glands lurked organisms more dangerous than those harboured by any other focus, he would soon be assembling cases in which treatment applied to the eyelids had been followed by dramatic amelioration of the dental state. He might even persuade his patients that they should go to bed with teeth uncleaned rather than neglect their lid-massage.

It may be well, however, to postpone this question of focal sepsis until we have considered some of the instances in which teeth and eyes are fellow-victims of (1) abnormal development, (2) trauma, (3) diseases of other organs and tissues, and (4) toxic hazards.

A. ASSOCIATED OCULAR AND DENTAL LESIONS

1. *Developmental defects* of the eyes and teeth are inevitable whenever there is widespread malformation of the head and face, but fortunately most of the resulting monsters are stillborn. More important from the practical standpoint are cases in which infantile lamellar cataract is associated with hypoplasia of the teeth. Theoretically these allied signs might be attributable to some defect in the germ-plasm—that is to say, they might be hereditary in the strictest sense; but most people interpret them as the effect of unfavourable intra-uterine influences, such as toxins derived from micro-organisms, or poisonous substances in the mother's food. Maternal diet can be the vehicle of damage not only through its noxious contents, but also by reason of deficiency. There might, for instance, be a shortage of certain essential amino-acids, vitamins or metals. Adequate calcium content is one well-recognised need during pregnancy, and the relationship of that element with the parathyroids is bound up with the influence of the latter upon the skeletal system. Parathyroid defect is closely linked with tetany and rickets, and the dental changes chiefly implicate the first molars together with the central and lateral incisors.

2. *Trauma.* One of the greatest therapeutic triumphs of modern times is the treatment of severe facial injuries, especially those accompanied by fracture of the upper-jaw. During the recent war

I visited the maxillo-facial units at Hill End, Park Prewett and East Grinstead, and also had the opportunity to see their successful end-results coming back into active service. Many a man hurtled against a wall in motor-cycle crashes would have been condemned to frightful disfigurement and enduring diplopia, had it not been for the skill of dental and plastic surgeons promptly administered. The ingenious devices whereby traction was applied to reinforce the action of splints after early reduction of those impacted maxillary fractures moved me to admiration, and there must be many medical men whose respect for the dental profession was enhanced by war-time contacts.

In the early stages of severe facial injury ophthalmic examination is needed with a view to ascertaining whether any immediate eye treatment is necessary, but thorough inspection is often impossible until swelling of the eyelids has abated. Later on the patient may require orthoptic and operative treatment for double vision due to weakness of one or more of the extra-ocular muscles, but spontaneous recovery from diplopia often ensues within a few weeks, if early manipulation by a dental expert has succeeded in restoring the alignment of the inferior orbital margin.

One possible result of maxillary trauma is an extension of sepsis from the teeth to the eyes, but the routes whereby infective material may travel will be considered later. Another possibility to be borne in mind is that ocular damage may be occasioned by a violent dental extraction. In this connection the myopic retina is particularly vulnerable. When we consider that the jolt of a starting train has been known to provoke retinal detachment, and that large haemorrhages may become evident on the surface of the fundus immediately after a sneeze, it is not surprising that similar havoc may accrue when jaws are wrenched against the resistance of muscular spasm. This last-mentioned state of affairs is apt to arise when a strong man undergoes incomplete dosage with nitrous oxide.

Before we leave the subject of trauma, it may be interesting to recall that a few of the dental surgeons attached to maxillo-facial units in the recent world war became expert in the construction of artificial eyes. In one instance I can testify to such skill on the part of a Service dentist, to whom I referred a number of cases needing prostheses. So far I have failed to trace any evidence of reciprocal virtuosity on the part of an ophthalmologist, and I doubt whether many of you would be inclined to delegate the building of your patients' dentures to an eye doctor.

3. *Diseases of other organs and tissues.* (*a*) *Endocrine dyscrasia.* Reference has already been made to the close relationship of the *parathyroids* with calcium metabolism, and we know

that other members of the endocrine orchestra can exert a profound influence upon dental and ocular welfare before and after birth. Thus the skeletal changes associated with *dyspituitarism* can interfere with the alignment of teeth, and the victim may also exhibit defects of the fields of vision due to pressure of the gland upon the optic chiasma or adjacent portions of the visual pathway.

The eruption of teeth is delayed in cretins, and further impairment is entailed by pressure from the heavy, splayed-out tongue typical of this disease, which in its turn is caused by hypoplasia of the *thyroid* gland. Further evidence that secretion from this gland affects the dental state is provided by the administration of thyroxin to experimental animals. Eruption of the incisors is thereby accelerated.

One disease that has often been found in association with widespread endocrine disturbance is *keratoconjunctivitis sicca*, a condition arising in middle life, and predominantly affecting women. It is characterised by sensations of dryness and grittiness of the eyes. Examination usually reveals irregularity of the corneal epithelium, together with small whitish strands of irregularly proliferating cells attached to the surface of the cornea. Absence of or diminution in the tears must be held partly responsible for the symptoms, but deprivation of the mucus normally secreted by small glands in the conjunctiva probably counts more. From the dental surgeon's standpoint the main importance of *keratoconjunctivitis sicca* is that similar desiccation usually occurs in the victim's mouth. Therefore she may become incapable of tolerating her dentures for more than a few minutes at a time.

(*b*) *Bone disease*. A number of bone diseases possess joint interest for dental and ophthalmic surgeons. *Acute osteomyelitis of the upper jaw* is one example which may arise in early infancy. Most people are agreed that ethmoidal suppuration is the commonest cause of orbital cellulitis among infants, but maxillary osteomyelitis, with or without preceding trauma to the mouth, should always be borne in mind as a possibility. Some of the reported cases have been fatal, but successful results have recently been claimed for penicillin therapy. Swelling and induration of the cheek on the affected side is a conspicuous sign, the temperature is high, and the infant usually looks very ill. When an abscess forms, it may point along the gum-line, on the palate, in the nose, or through the lower eyelid. Proptosis and restriction of ocular movement on the affected side are prominent features until the pus is absorbed or evacuated.

In *osteogenesis imperfecta* we find blue sclerotics associated with abnormal fragility of the bones, so that fracture of the lower jaw may arise from a relatively slight blow. The upper and lower jaw

may both be implicated in *Schüller-Christian xanthomatosis*, a disease which may produce proptosis of the eyeballs in early childhood. Slight fever, secondary anaemia, and diabetes insipidus due to hypopituitarism are other items in the clinical picture, and the diagnosis is clinched by radiography of the skull, the flat bones displaying punched-out areas of rarefaction. *Albers-Schönberg's disease* tends to run in families, and consists of diffuse osteosclerosis. One of its characteristic results is bilateral optic atrophy due to encroachment of the new-formed bone upon the optic canal. Delayed dentition and early caries are also noted, and occasionally osteomyelitis of one or both jaws supervenes. In *oxycephaly* the small size of the maxilla may interfere with dental development by crowding the teeth together. Delayed dentition is also a feature of *hereditary cleido-cranial dysostosis*, a disease in which defective ossification of the skull-vault lends to depression of the orbital roofs, and that in its turn produces exophthalmia.

Two bone diseases of later onset are worthy of mention. *Leontiasis ossea* is particularly apt to induce hideous deformity, because the two sides of the face are seldom symmetrically involved. Lateral and forward displacement of one or both eyes may become evident, and vision may be curtailed by pressure upon the optic nerve in its bony canal. Similarly the teeth may sustain damage and displacement from irregular encroachment of bone in the upper and lower jaws. In advanced cases the dental state may be aggravated by hindrance to closure of the mouth. *Paget's disease* is a familial affection of later life, often associated with generalised arteriosclerosis. Immense thickening occurs in the long and flat bones, and X-ray photographs in an advanced case reveal characteristic areas of adjacent absorption and calcification. In some cases the onset is exceedingly slow, and indeed this disease may stay mainly confined to one bone for many months. Probably the tibia is the commonest single bone to display Paget's type of thickening, but cases have been described in which signs were first exhibited in the maxilla. Sooner or later the orbital walls begin to thicken, and deposition of bone in the optic canal leads to progressive optic atrophy.

Skeletal and endocrine diseases have been briefly reviewed, because they supply so many striking instances of associated dental and ocular disturbance. Other kinds of linkage might readily be assembled, but here it will suffice to stress the interdependence of organs and tissues throughout the body. Clearly the eyes and the teeth are likely to last longer in people blessed with a sound cardiovascular system, and yet the finest heart and blood-vessels in the world cannot keep these organs healthy unless their nervous connections are intact—because all nerves are in a real sense trophic.

Nor can the nervous and circulatory structures function well, unless every essential item of diet is supplied in appropriate quantity. Thus the problem of causation in an apparently simple lesion may be complex beyond the bounds of imagination. Whatever facts may be elicited by clinicians working in close co-operation with dietetic experts, pathologists, radiologists and other specially trained helpers, we cannot explain every aspect of disease, because the mode of response to identical noxious stimuli may be largely conditioned by genetical factors impossible of assessment.

4. *Toxic hazards.* A few examples will serve to show how the eyes and teeth share susceptibility to a number of poisons. *Lead* can play havoc with the optic nerve and the jaws, but improved plumbing together with preventive industrial measures have almost eliminated this former scourge. Necrosis of the orbit and jaws from *phosphorus* is also rare to-day. Indeed so much knowledge has accumulated concerning the injurious by-products of mines and factories, that important chemical lesions seldom arise unless workers are unintentionally exposed to some new organic compound, the pharmacological effect of which is not yet appreciated. Many volumes have been written upon the deleterious effects of *nicotine* upon the eyes and teeth, and we cannot expect to find unanimity of opinion upon this question for many a year to come. Few would deny that excessive smoking injures the buccal mucous membrane, and incidentally the teeth, but wide individual variations in tolerance make one man's moderation another man's excess. Tobacco amblyopia is a real threat to heavy smokers in later life, and necessitates complete abstinence from smoking, but other factors besides tobacco play a part in its development.

B. The Teeth as a Source of Ocular Infection

It is abundantly clear that some disease-processes can spread from the teeth to the eyes, but wide disagreement exists concerning the proportion of dental infection compared with that from other sources. Theoretically dental disease could be communicated to the eye by direct extension through bone and other connective tissue, or along the ramifications of nerves, or *via* the veins and lymphatic vessels. Toxins might enter the blood-stream direct from diseased teeth and afterwards find their way into the ocular arteries; or the noxious material might travel indirectly, being absorbed into the blood-stream *via* the alimentary canal. Nor would it seem impossible for dental toxins to reach the inferior meatus of the nose, whence they can travel up the tear-passages into the conjunctival sac. Probably all or most of these pathways have been traversed by infective material, but dissemination by the blood-stream is

generally regarded as the most important, except in cases which plainly show direct spread.

Among the conditions which ophthalmologists have regarded as due to dental disease are orbital cellulitis, dacryocystitis, blepharitis and other inflammatory disorders of the eyelids, conjunctivitis, episcleritis, keratitis with or without ulceration, iridocyclitis, choroido-retinitis, venous thrombosis, cataract and lesions of the optic nerve. In this connection particular stress has been laid upon iridocyclitis, and the reasons are not far to seek. Cases of iridocyclitis exhibit astonishing variations in severity and duration, and incidentally, of course, in their apparent response to treatment. Some show slight initial changes, but keep on recurring until the eye is ruined. Others severely affected at the outset clear up rapidly, and then go on for years without further trouble. It follows therefore that *any* treatment will appear to produce miraculous results in a certain number of cases. Enthusiasts naturally resent being told that they have mistaken mere sequence for a cause-and-effect relationship, but such reminders are wholesome and necessary. In dealing with so variable a disease as iridocyclitis, we have to look askance at alleged therapeutic triumphs until the method in question has proved effective in a long series of carefully followed-up cases.

Now the theory of focal infection, so long as it is firmly upheld, can be advanced as a coherent explanation for nearly all kinds of endocular inflammation, and positively disproved in hardly any instance. Let us imagine a case of iridocyclitis being examined in consultation with a colleague firmly convinced that teeth are nothing but fountains of sepsis. No clinical evidence of dental disease can be found. Then he points out that a healthy-looking tooth may be likened to a whited sepulchre. X-ray photographs are now prepared, but fail to reveal any abnormality. Our friend now proceeds to quote authority for his belief that radiographically negative teeth are by no means incapable of spreading disease elsewhere in the body. Thus he persuades the patient to part with his teeth, and one of three things happens:

(*a*) The eye recovers. That clinches the argument.

(*b*) The eye gets worse, but that goes to prove how wise it was to insist upon extraction. Exacerbation analogous to a Herxheimer reaction is readily interpreted as the effect of an extra dose of toxin flung into the circulation while the teeth were being dislodged.

(*c*) No change is noted in the eye. Therefore the offending teeth must have set up a secondary focus of infection before the patient had finally decided to part with them. Probably the prostate is now to blame, though admittedly palpation reveals no abnormality of that organ. Yes, but chronic prostatitis may drag on for

years without producing any localising signs or symptoms. Prostatectomy is now performed. Still the iridocyclitis grumbles on, because [*sic*] the original focus has impaired the patient's power of resistance, and he is now susceptible to the action of lesser toxins, which he would have taken in his stride had his defences not been undermined by those teeth.

Let me repeat that such a zealot cannot be decisively confuted at any stage in his argument, and my reason for setting-out that grim sequence of events is that I have often heard people argue on those lines. With very little modification the same kind of reasoning can be adduced to prove that any particular disease is an outburst of allergy—whatever that may be.

It would appear, however, that the concept of dental infection as a paramount factor in the production of intra-ocular disease has lost ground. Several research workers have failed to repeat the earlier work on apical infection, and it has been suggested that oral contamination would explain many disquieting statistics about the prevalence of streptococci in the teeth. It has also been shown that radiolucent areas around dental roots are not necessarily a sign of disease, and more and more people have come to believe that teeth should be treated on their own merits—or demerits, as the case may be. Was it not Don Quixote who said: "A diamond is not as precious as a tooth." My own attitude towards the relation of dental with ocular disease can be summarised as follows:

(1) Harmful substances can certainly pass from the teeth to the eyes, and possibly in the reverse direction.

(2) I do not believe that the teeth are mainly to blame in more than a small minority of the cases of ocular disease.

(3) The causation of disease is infinitely more complex than most people realised three or four decades ago, when the doctrine of focal sepsis was approaching the peak of its popularity.

In fairness to the dental surgeon, it should be pointed out that the indiscriminate slaughter of teeth as a measure of desperation in cases not responding to other forms of treatment has nearly always been at the instigation of medical men. Consider rheumatoid arthritis and recurrent iridocyclitis, which have several important features in common. Both are productive of much pain and disability. In each of these diseases the cause is complex and imperfectly known, so that the stage is set for the enthusiast whose attention is disproportionately directed to one aspect of the problem. Some cases of iridocyclitis display features which an experienced clinician can recognise as pathognomonic or at least strongly suggestive of syphilis, gonorrhoea, tubercle and various other diseases. Corroboration is in many instances supplied by the

manifestations of a similar pathology elsewhere in the body. Nevertheless it remains true that, in any large series of people suffering from iridocyclitis, there will be a considerable percentage to whose origin there is no clue, unless the observer happens to be a fanatic. The proportion of unsolved cases is greater among female than among male victims, largely because typical gonococcal iridocyclitis seldom arises in women.

CO-OPERATION BETWEEN DENTAL AND OPHTHALMIC SURGEONS

Theoretically an eye capable of resisting certain toxins entering the circulation from unhealthy teeth might be rendered vulnerable in consequence of trauma. Therefore many ophthalmologists, unless the case is urgent, deliberately refrain from performing an intra-ocular operation until any necessary dental treatment has been completed. Others maintain that this precaution makes no appreciable difference to the prognosis, and some go so far as to say that post-operative complications are rendered more likely by the flood of toxic matter dislodged by dental extraction, and they point out that removal of any considerable number of teeth is often followed by general lowering of a patient's power of resistance. Perhaps the best solution is to treat every case as a separate problem, but certainly it seems a reasonable precaution in all except urgent cases, to postpone intra-ocular surgery pending dental treatment, if gross oral sepsis comes to light. It would also seem wise, in cases requiring multiple tooth-extraction, to arrange for a few weeks' convalescence before the eye operation is performed.

There are many other fields for fruitful co-operation between these two branches of surgery. During the World War of 1939-45 important pieces of research had to be shelved in favour of activities calculated to produce immediate results, and specialised training was perforce curtailed. There is, however, another side to the picture. Under the impact of war, opportunities arose for trying-out new methods of treatment on a large scale, and the maxillo-facial units, of which mention has already been made, enabled ophthalmic and dental surgeons to realise how many of their problems overlap. Now it seems certain that technique will continue to grow more specialised in every branch of medicine and surgery, and all such improvements count as progress. Neverthless they sound a note of warning. Each successive refinement in technique is a potential barrier or path of divergence between one kind of specialist and another, so that we must be vigilant to keep an eye upon the borderline territory—yes, and to maintain a firm *bite* upon joint problems. Long ago Saint Lucia was singled out as the patroness of the eye, and a similar rôle was granted in the realm of dentistry to Saint

Apollonia, but some of the ancient English people looked upon Saint Lucia as the luminary responsible for both sets of organs. Let me conclude with the hope that this primitive belief was of good augury, and that it will serve to emphasise the significance of our eye-teeth.

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CONCENTRATION IN THE AQUEOUS OF VARIOUS SULPHONAMIDES AFTER SYSTEMIC ADMINISTRATION*

BY

ARNOLD SORSBY

LONDON

THE earlier experimental studies of Bellows and Chinn (1939 and 1941), Pinkoff (1939), Meyer, Bloch and Chamberlain (1941), Liebman and Newman (1941), and Scheie and Souders (1941), have established that sulphanilamide and sulphapyridine penetrate readily into the interior of the eye on oral administration, whilst sulphathiazole has a poor penetration. The penetration of sulphadiazine was found to be high (Scheie and Souders, 1941; Liebman and Newman, 1941). There do not appear to be any studies on the newer sulphonamides such as sulphamezathine and sulphamerazine. For clinical purposes sulphanilamide and sulphapyridine can be ignored as they are no longer widely used owing to their relative toxicity. In practice the choice to-day is

* Dedicated to Professor J. Meller.

largely limited to sulphadiazine, sulphamerazine, sulphamezathine and sulphathiazole. The present study was undertaken to assess the relative penetration of these sulphonamides into the aqueous.

Animals used. The penetration of sulphadiazine, sulphamerazine and sulphamezathine into the aqueous was determined in rabbits. The penetration of these sulphonamides, as also of sulphanilamide and sulphathiazole, was studied in the rat.

Technique. In the rabbit a dose of 100 mg. per kg. of bodyweight of sulphadiazine, sulphamerazine and sulphamezathine was given intravenously, and the concentration of these different sulphonamides was assessed in the plasma, blood, and aqueous. In the rat a dose of 150 mg. per kg. was given orally. The values recorded are in each case averages of readings in four animals for each time period shown.

CONCENTRATION IN THE AQUEOUS OF THE RAT

Figs. 1-5 show the concentrations obtained in the plasma, blood and primary aqueous from the administration of each of the five sulphonamides studied, sulphanilamide, sulphadiazine,

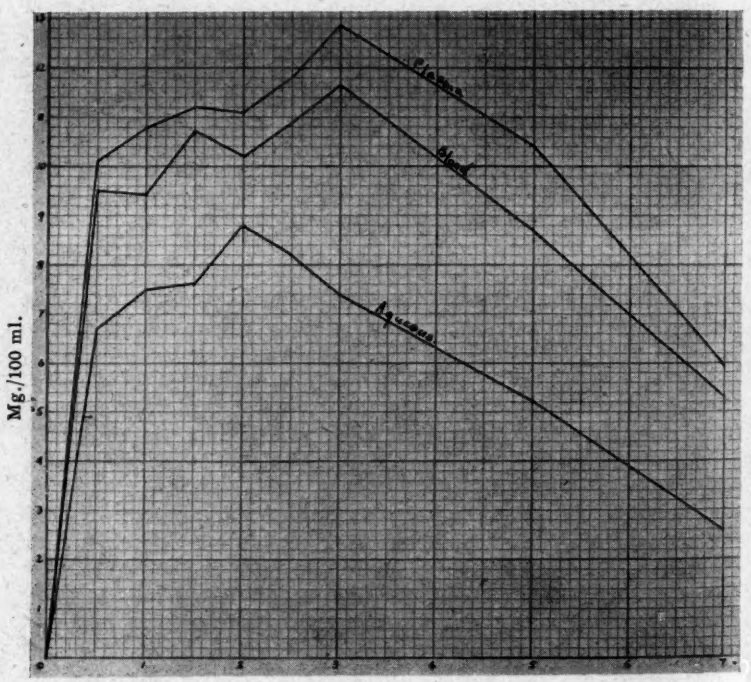

FIG. 1.—Sulphanilamide—150 mg /kg. orally in rats.

sulphamerazine, sulphamezathine and sulphathiazole. Fig. 1 confirms earlier observations that with sulphanilamide high immediate levels are obtained in plasma, blood and aqueous. It will be seen that at 7 hours the aqueous level is still as high as 2·6 mg./100 ml. Fig. 2 shows that sulphadiazine has a rather lower level, whilst Fig. 3 shows a somewhat higher level with

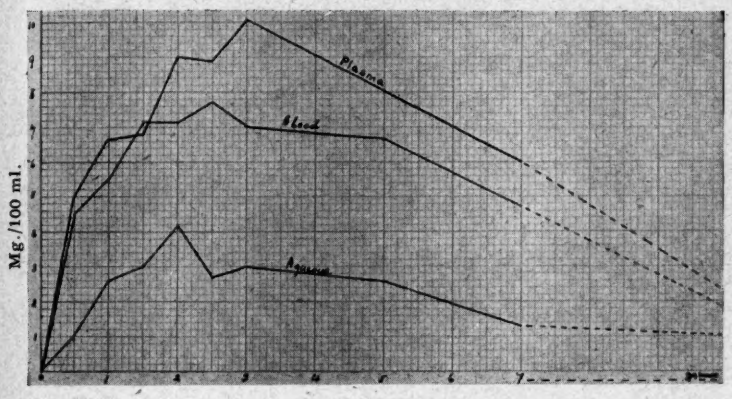

FIG. 2.—Sulphadiazine—150 mg./kg. orally in rats.

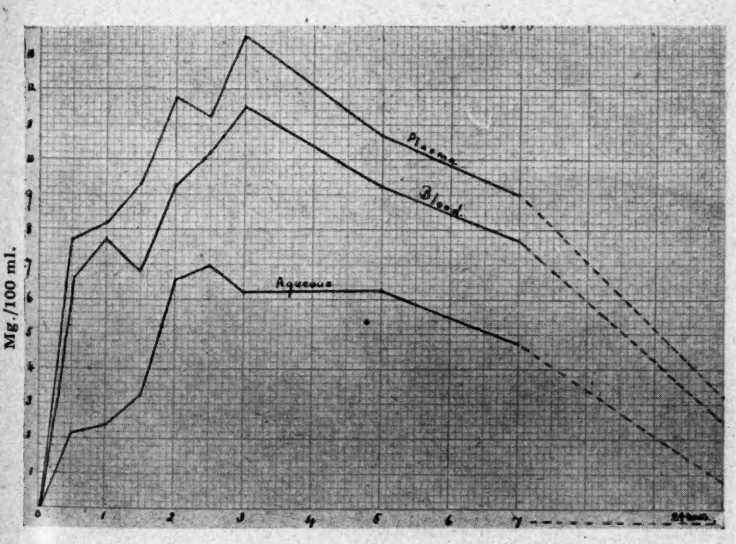

FIG. 3.—Sulphamerazine 150 mg./kg. orally in rats.

sulphamerazine. The levels for sulphamezathine (Fig. 4) are lower than for sulphamerazine and not dissimilar to those for sulphadiazine. Fig. 5 shows a consistently low level for sulphathiazole, with total disappearance of any concentration by

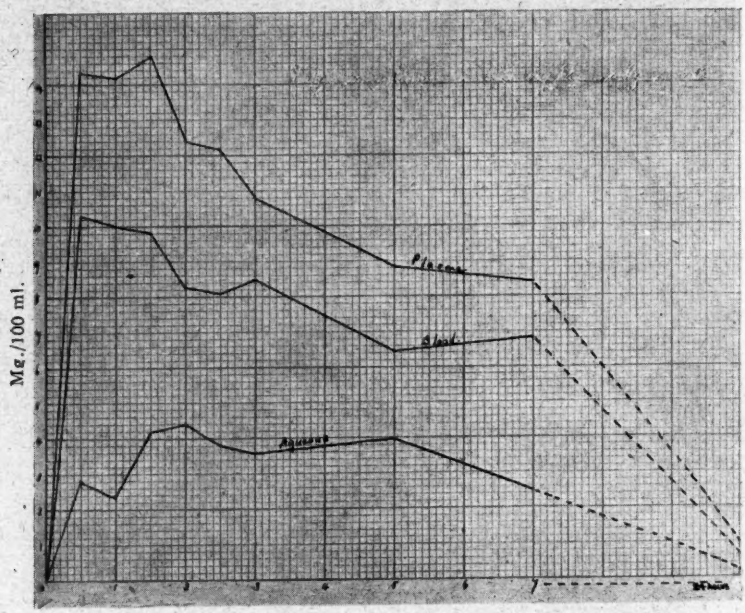

FIG. 4.—Sulphamezathine—150 mg./kg. orally in rats.

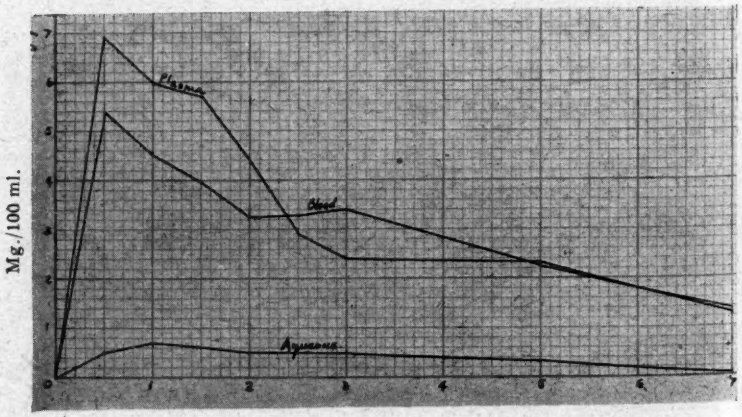

FIG. 5.—Sulphathiazole—150 mg./kg. in rats.

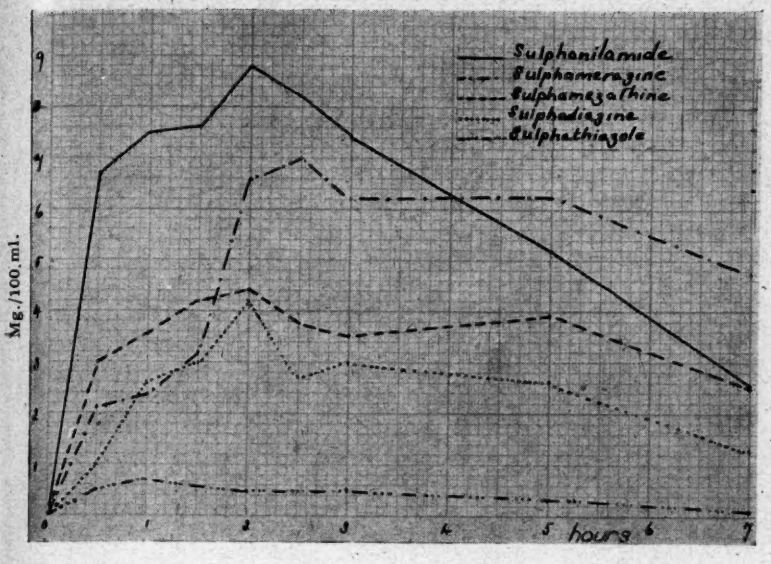

FIG. A.—Sulphonamides—150 mg./kg. orally in rats. Comparison of the aqueous concentration.

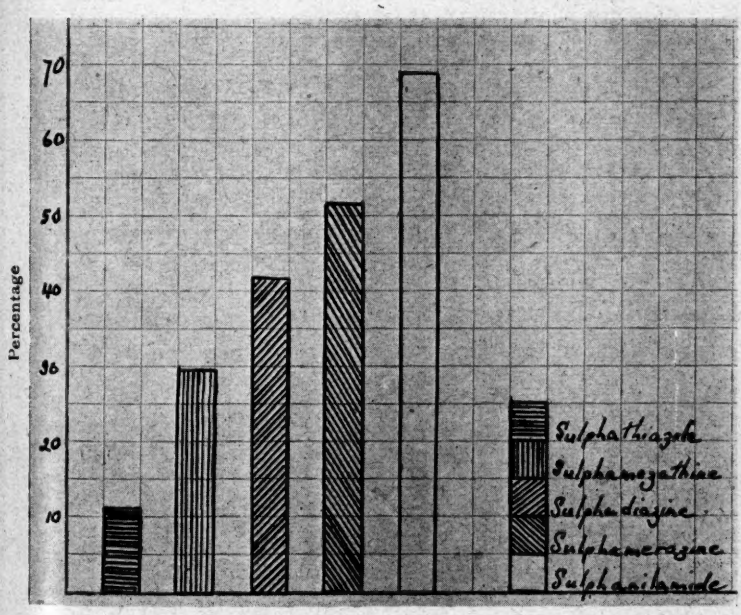

FIG. B.—Sulphonamides—150 mg./kg. in rats.

Highest aqueous concentration as percentage of highest plasma concentration for each of the five sulphonamides.

TABLE I

Comparative levels of concentration of five different sulphonamides in the aqueous and plasma of the rat on oral administration of a single dose of 150 mg. sulphonamide per kg. bodyweight.

Sulphonamide	Aqueous				Plasma		Highest aqueous level as percentage of highest plasma level
	Highest Concentration		Concentration mg/100 ml.		Highest Concentration		
	Quantity	Time	At 7 hours	At 24 hours	Quantity	Time	
Sulphanilamide	8·8 mg/100 ml.	2 hrs.	2·6	—	12·8 mg/100 ml.	3 hrs.	68·8
Sulphadiazine	4·2 „	2 „	1·3	1·0	10·0 „	3 „	42·0
Sulphamerazine	7·0 „	2½ „	4·8	0·8	13·5 „	3 „	51·9
Sulphamezathine	4·4 „	2 „	2·5	0·3	14·8 „	1½ „	29·7
Sulphathiazole	0·7 „	1 hr.	0	—	6·9 „	½ hr.	10·1

the 7th hour. At 24 hours there is no sulphanilamide at all in the aqueous, whilst the levels for sulphadiazine and sulphamerazine are around 1 mg. per 100 ml., with an even lower reading for sulphamezathine. The absolute aqueous concentrations of these five sulphonamides are contrasted in Fig. A, whilst Fig. B shows the highest aqueous levels as percentages of the highest plasma concentration of each of the five agents. The salient features brought out may be summarised in the table.

It will be seen that on all counts sulphathiazole is the least satisfactory. Of the remaining four agents sulphanilamide and sulphamerazine both reach considerable aqueous levels, 8·8 and 7·0 mg./100 ml. respectively at their peak, (2 hours and 2½ hours respectively), as against 4·2 and 4·4 mg./100 ml. respectively, (both at 2 hours) for sulphadiazine and sulphamezathine. At 7 hours sulphamerazine still has a relatively high level, 4·8 mg./100 ml., whilst sulphamezathine has double the level of sulphadiazine, 2·6 mg./100 ml. against 1·3.

CONCENTRATION IN THE AQUEOUS OF THE RABBIT

In the rabbit the plasma, blood and aqueous values for sulphadiazine, sulphamerazine and sulphamezathine after intravenous injection are shown in Figs. 6-8, and the aqueous values are contrasted in Fig. C. Fig. D shows the highest aqueous levels as percentages of the plasma levels at 30 minutes after injection. The salient features are shown in the following summary table.

TABLE II

Comparative levels of concentration of three different sulphonamides in the aqueous and plasma of the rabbit on intravenous administration of 100 mg. sulphonamide per kg. bodyweight.

Sulphonamide	Aqueous				Highest aqueous level as percentage of plasma level at ½ hour
	Highest Concentration		Concentration mg/100 ml.		
	Quantity	Time	At 3 hrs.	At 7 hrs.	
Sulphadiazine	6·0	1½ hrs.	1·8	0·2	53·6
Sulphamerazine	3·5	½ hr.	1·1	0·2	52·3
Sulphamezathine	5·0	½ „	0.6	0·0	61·0

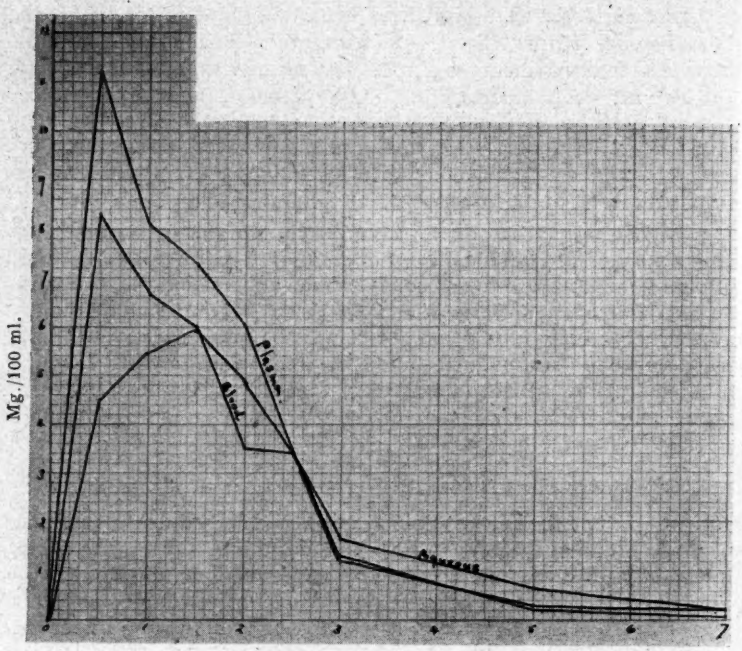

FIG. 6.—Sulphadiazine—100 mg./kg. intravenously in rabbits.

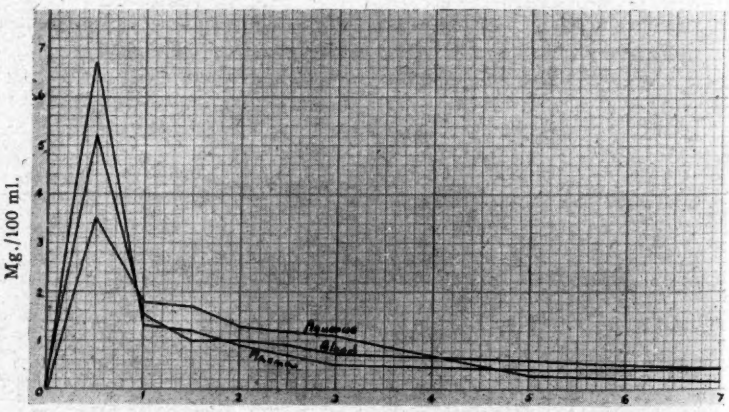

FIG. 7.—Sulphamerazine 100 mg./kg. intravenously in rabbits.

It is seen that the highest absolute aqueous concentration is reached with sulphadiazine, and that sulphamezathine gives a higher level than sulphamerazine. Sulphamezathine appears to be most rapidly eliminated, but it gives the highest ratio of aqueous/plasma concentration.

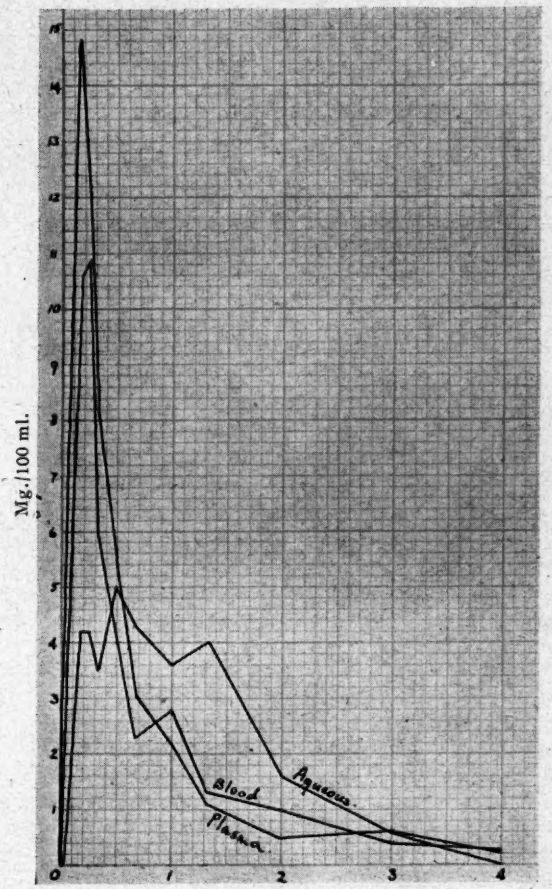

FIG. 8.—Sulphamezathine 100 mg./kg. intravenously in rabbits.

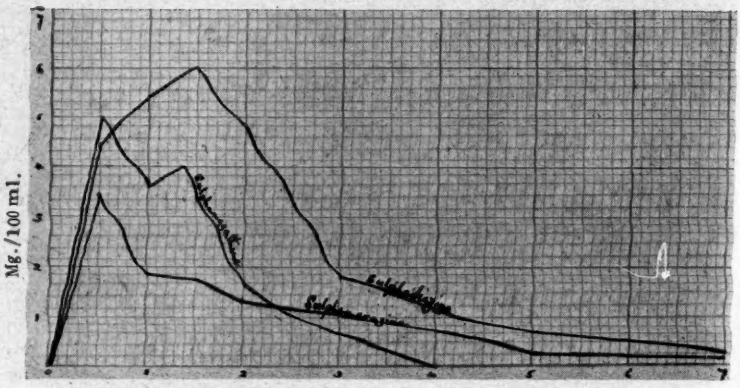

FIG. C.—Sulphonamides—100 mg./kg. intravenously in rabbits. Comparison of the aqueous concentration.

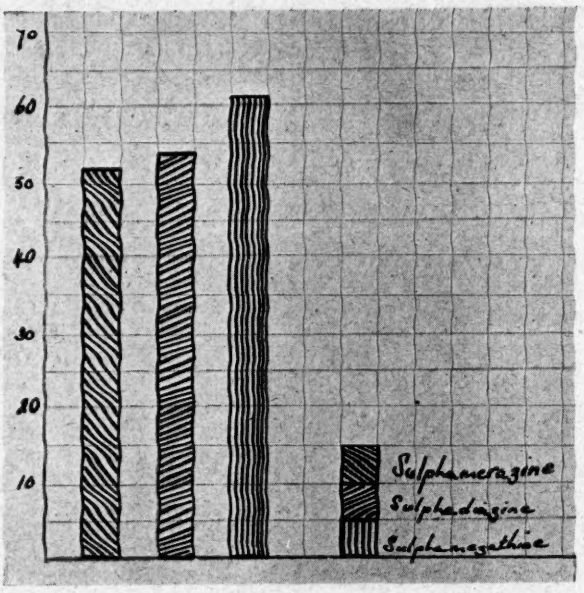

FIG. D.—Sulphonamides—100 mg./kg. intravenously in rabbits.

Highest aqueous concentration as percentage of highest plasma concentration for each of the three sulphonamides.

DISCUSSION

With the reservation that whilst neither absolute values, nor ratios of aqueous concentration to plasma concentration, nor the time factors established in the experimental animal can be applied uncritically to man, the following conclusions are warranted.

(1) *Absolute values in the aqueous.* Sulphathiazole is the least satisfactory. In the rat both sulphanilamide and sulphamerazine give higher values than sulphadiazine and sulphamezathine, but in the rabbit both sulphadiazine and sulphamezathine give higher levels than sulphamerazine.

(2) *Ratio of aqueous concentration to plasma concentration.* Here, too, sulphathiazole is least satisfactory. In the rat both sulphanilamide and sulphamerazine give higher ratios than sulphadiazine and sulphamerazine, but in the rabbit there is no substantial difference between sulphamerazine and sulphadiazine, whilst sulphamezathine gives a higher value than either.

(3) *Rate of excretion from anterior chamber.* In the rat at 7 hours after oral administration the aqueous concentration is nil with sulphathiazole, and 4·8 mg./100 ml. with sulphamerazine. Intermediate and successively diminishing values are recorded with sulphamezathine, sulphanilamide and sulphadiazine. In the rabbit the values at 3 hours after intravenous administration are highest for sulphadiazine, lowest for sulphamezathine and intermediate for sulphamerazine.

Eliminating sulphanilamide from consideration because of its toxicity, the one clear conclusion that emerges is the unsuitability of sulphathiazole for use in intra-ocular infections. Of the remaining three sulphonamides, sulphamezathine appears to be rather better than sulphadiazine, whilst sulphamerazine is clearly superior to sulphamezathine judging by the levels and persistence obtained in the rat—a superiority not apparent in the rabbit.

SUMMARY

1. Sulphonamide concentrations in the aqueous were determined for sulphanilamide, sulphadiazine, sulphamerazine, sulphamezathine and sulphathiazole after oral administration of 150 mgm. per kg. bodyweight in the rat. Similar determinations were carried out for sulphadiazine, sulphamerazine and sulphamezathine administered to the rabbit intravenously in doses of 100 mg. per kg. of bodyweight. Corresponding values were established for blood and plasma.

2. In the rat the highest concentration in the aqueous was given by sulphanilamide, with successively lower readings for

sulphamerazine, sulphamezathine, sulphadiazine and sulphathiazole. As for persistence, as measured by the presence of sulphonamide in the aqueous 7 hours after administration, sulphamerazine gave the highest value with successively decreasing values for sulphamezathine, sulphanilamide, sulphadiazine and sulphathiazole. Assessment of the highest aqueous level as a percentage of the highest plasma level showed the highest value for sulphanilamide, with successively lower values for sulphamerazine, sulphadiazine, sulphamezathine and sulphathiazole.

3. In the rabbit the highest concentration in the aqueous was given by sulphadiazine, with successively lower values for sulphamezathine and sulphamerazine. Sulphadiazine also proved to be the most persistent as assessed by the aqueous concentration at 3 hours. The highest aqueous/plasma ratio was shown by sulphamezathine.

I am greatly indebted to Dr. A. Spinks, of the Research Laboratories. Imperial Chemical Industries Ltd., Manchester, for assistance in carrying out the experiments.

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THE SIGNIFICANCE OF OCULAR COMPLICATIONS FOLLOWING VACCINATION*

BY

EMANUEL ROSEN

NEWARK, N.J.

THE occurrence of ocular complications shortly after vaccination, of the secondary or indirect variety, is not new, for it has been reported in ophthalmic literature about twelve times. The observation of a greater number of cases in a period of two months would indicate that these complications should provoke greater interest than they have hitherto received. This secondary type of ocular complication is so named in order to differentiate the accidental vaccinial inoculation produced by first scratching the

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pustule and then touching the eyelid, from the ocular complication which is endogenous and usually part of a post-vaccinial encephalitic phenomenon.

While at Fort Benning, Georgia, in 1945, I observed an interesting case of interstitial keratitis associated with vestibulo-auditory symptoms following vaccinia. This case was similar to four cases reported by David Cogan[4], which introduced a new syndrome of unknown aetiology, namely, non-syphilitic interstitial keratitis associated with vestibulo-auditory symptoms. After studying these cases it appeared that our case was one of the same syndrome, save that the patient's symptoms developed seven days after vaccination. It seemed that this syndrome might be a variety of post-vaccinial encephalitis, since both the fifth and eighth cranial nerves were involved. The syndrome was bilateral, recurrent and reversible. The case report in some detail is as follows:—

The patient was a 30-year-old male who had served in the armed forces for over four years. The onset of acute illness occurred on March 13, 1945, one hour after the noonday meal. The initial symptom was nausea which was followed shortly by retching and then by projectile vomiting. After vomiting had ceased the patient noticed a persistent dull nuchal headache which did not keep him from his work that afternoon, throughout which it remained unchanged. There were no chills, dizziness or fever at this time. The patient slept well that night, but on awakening the next morning he felt dizzy, as though the bed were rotating. This sensation vanished in a few hours, so that he was able to report to work at the usual time. Again, following a frugal noonday meal, the symptoms of the previous day returned, together with an oppressive tightness about the neck. The dizziness recurred, and he returned home, where he spent a comfortable night. On this second day the headache did not recur. When he got up on March 15, the patient was still dizzy and somewhat faint. He was admitted by ambulance to the hospital, where followed a mild bout of retching. The only symptom for the first week was persistent dizziness, more pronounced when the patient stood up. At no time was the temperature abnormal. His past history indicates that the patient has had several mild virus diseases, including several slight attacks of herpes labialis. Mumps, measles, scarlet fever and chicken-pox were all contracted without any serious sequelae. On March 6 the patient was vaccinated with vaccinia virus, and was also given a stimulating dose of triple typhoid. There was no systemic or local reaction to the vaccination or to the typhoid injection, and the incident had been forgotten.

On admission the physical examination was reported as normal. The temperature was 98°, the blood pressure was 114/86, and the pulse rate was 86. There were no neurological signs and no physical findings other than vertigo. The urine examination was negative. A blood count performed upon the day of admission showed a leucocytic count of 11,700 of which 72 per cent. were "polymorphs" and 28 per cent. "lymphocytes." Several subsequent blood counts were performed with an 8,000 to 15,000 leucocytic variation, and maintenance of the above percentage for the differential count. Routine tests for syphilis, undulant fever and tularemia were reported as being negative. Spinal fluid studies were made ten days after the onset of the illness, and were reported as normal. X-rays of both the skull and the chest were negative. Because of the persistence of vertigo without associated symptoms further consultation was sought along otological and neuropsychiatric lines. The neurological examination was negative. The psychiatric examination is summarized in the following paragraph:—"This officer appears to be a passive neurasthenic individual. In the service he failed to gain a commission because of lack of physical performance and leadership of men

in a combat type of duty. He was given a form of work following this failure which was technically and psychologically very acceptable to him. As a result of his work he gained a warrant officer's status which to him was very gratifying. While on leave, he was, without previously being informed, relieved of his command and placed upon an "available" list. He took this in a normal manner consciously, and reacted with "well a soldier is never put." Psychologically, however, this was a serious failure upon his part. With this news there was the threat of combat theatre duty and separation from his wife, upon whom he depended a great deal emotionally. He reacted to the situation in the only manner he is capable of, namely, an acute episode of hysteria. His neurasthenic features have existed for many years and manifested themselves early in his military career. Diagnosis:—psychoneurosis and neurasthenia.

Ear, nose and throat studies were of indeterminate value. Upon rechecking the history it was learned that two years earlier the patient had noticed buzzing in his ears shortly after swimming. This buzzing had only lasted two days. One week after the onset of acute vertigo the patient complained of transient auditory disturbances. He described two distinct kinds: one was of the "cockleshell" variety; the other resembled the hum of an undialled telephone. The otologist reported that the results of his audiometric and labyrinthine studies were unreliable, transitory, indeterminate and contrary to expectation. During the second week the transient auditory symptoms appeared. Ocular manifestations arose about the first of April, being quite mild at the onset. The right eye was first involved. There was no pain and no secretion. There was a mild conjunctival injection and a slight sensitivity to light. After instillation of a mild astringent (zinc sulph. ¼ per cent.) the eye appeared to improve, and remained comfortable for about ten days, after which time similar but more severe symptons recurred. Examination at this time disclosed slight aqueous flare, thickening of the cornea, several folds in Descemet's membrane, and many "craters" visible in the zone of specular reflection. There were also several small foci of opacification in the corneal stroma. At various places the limbal vessels were beginning to push into the corneal substance superficially. Under atropine drops locally, and typhoid therapy intravenously, the right eye gradually cleared in about three weeks, but by this time a similar picture had begun to develop in the left eye. Attacks continued to shift from one eye to the other, each attack lasting about one week, and then clearing without any residuum. The attacks were unrelated to any systemic manifestation. The events leading up to the patient's hospitalization, along with the neuropsychiatric findings and the presence of conjunctival secretion, even when a definite keratitis existed, aroused the suspicion of malingering. The patient was kept under observation, and there was a gradual improvement over many months. In this period there were several recurrences, but eventually all ocular and otologic symptoms subsided.

From this case report it seemed apparent that since ophthalmology deals with fifty per cent. of the cranial nerves, and since post-vaccinal encephalitis is a cranial nerve involvement, the ophthalmologist should be in an excellent position to see cases of post-vaccinial encephalitis at an early stage. Looking upon the eye as a bud from the brain, in whose interior one can deduce events occurring in the brain, particularly as regards vascular structures, it seems that there is further evidence of this ocular localization in complications of post-vaccinial encephalitis. The ophthalmologist may well detect certain vascular phenomena in the eye—for example, in the avascular cornea—and thus solve the problem which for so many years has eluded the clinical investigator seeking to explain the aetiology of post-vaccinial encephalitis. Changes in the optic nerve-head from pressure disturbances, inflammation and congestion, are not the only possibility. Direct

observation of the blood-vessels may be of value when the blood itself is altered, and the importance of the avascular cornea for observation of allergic phenomena cannot be over-emphasized, as shown by the work of Rich and Folis, 1940[9], whose studies of allergic phenomena in such tissues led them to believe that sensitization is due to the capillaries at the corneal limbus, not to corneal tissue *per se*. In animals previously sensitized, serum injected into the cornea produced inflammatory changes at the limbus. If, however, one eye had an artificially vascularized cornea, serum introduced into the cornea of a sensitized animal produced a haemorrhagic area within the corneal stroma itself at the terminus of this acquired vascularization.

A second case which we observed has a bearing upon the experiments of Rich and Folis.

Mr. J.K., age 37 years, was first seen at Camp Lee, Virginia, in the Fall of 1944 because of a severe metaherpetic keratitis in the left eye. This was his third attack. The lesions responded to treatment very slowly, requiring ten weeks of hospitalization before any permanent improvement was effected. Then he was discharged, and returned to duty. He remained free from eye symptoms until two weeks after vaccination in May, 1947, when the left eye became inflamed and painful. Examination revealed an inflamed cornea which was at least doubled in thickness. There was a general greyness over most of the corneal surface. The conjunctiva was intensely injected. There were many folds in Descemet's membrane. The optical section under the narrow beam looked very like a section through a washboard. One vessel ran deeply into the substance of the cornea, starting at nine o'clock. At first the activity seemed limited to the corneal substance just beyond this new vessel. During the acute period the iris could not be seen. Within the substance of the cornea there were several small infiltrates spindle-shaped in cross section. The acute process continued for several weeks, and gradually subsided.

A review of the literature on post-vaccinial encephalitis indicates that the allergic theory cannot be lightly dismissed. Putnam[21], Finley[7], Davidoff[5], Flexner[8], Glanzmann[12] and others believe that post-vaccinial encephalitis is an allergic response, whose incubation period is definitely related to the exanthem. The incubation period may be accelerated, and has been shown to be so in cases of revaccination. The symptoms of post-vaccinial encephalitis usually appear on the eleventh day, but in revaccination they may arise as early as the seventh day. I believe that this incubation period or interval following inoculation is more important than the symptomatology greatly stressed in so many writings. The fact that the patient develops coma, diplopia, nausea, headache, etc., is not nearly so important as the fact that these symptoms appear seven, eight, nine, ten or eleven days after vaccination. Therein lies the most important single finding in a variegated disease which for years has been so baffling.

A review of every autopsy available, both of post-vaccinial encephalitis and of the post-exanthematous encephalitides, made it

clear that one was dealing with the same pathological entity—whether of post-measles, post-pertussis, post-influenzal or the other virus diseases common in childhood. It is not difficult to understand why, for so many years, this problem has been a baffling one. The neuropathological picture in any of these diseases cannot be differentiated by the most competent investigator. On the other hand, when one considers the difficulties encountered in diverse staining techniques of nerve tissue, one can understand the variation in the reports of pathological studies concerning this group of diseases. One striking aspect revealed by this review of post-vaccinial encephalitis is the close relationship between the exanthematous encephalitides and acute multiple sclerosis. There are several ocular observations in support of this relationship. Thus Von Herrenschwand in 1939[24] wrote about ocular complications in post-vaccinial encephalitis. In 1912 he had reported a case of a six-year-old child who developed a post-vaccinial bilateral sixth nerve palsy. In his second report (1939) he listed three new cases, each of which came to autopsy. The patients were all about eight years old. Encephalitis occurred seven to ten days after vaccination, and death followed in two to three weeks. Clinical eye studies were not recorded in these cases, but autopsies including sections of the eye were performed with interesting results. In the first case there was an internal and external hydrocephalus with recent haemorrhage below the dura upon each side of the skull. Both trigeminal nerves and their sheaths were oedematous. The histological picture suggested an allergic response. A bilateral perineuritis of the optic nerve was present. The *post mortem* examination of the second case was most interesting as regards the ocular findings. The histopathological picture was an early retrobulbar neuritis, a condition which rarely comes to autopsy unless death ensues from some other cause. Von Herrenschwand believed that the presence of continuous circular lines of connective tissue within the vein was characteristic of post-vaccinial neuritis, and from this feature one could rule out other forms of encephalitis. Perhaps this concept of retrobulbar neuritis as determined by Von Herrenschwand's histopathological investigation in cases of post-vaccinial encephalitis, and the suggestion that we are dealing with an early allergic response may fit into the picture portrayed by Benedict[2] in his studies upon retrobulbar neuritis. Certainly it is no coincidence that retrobulbar neuritis terminates as multiple sclerosis (Benedict[2]), and that multiple sclerosis resembles the post-vaccinial encephalitis histopathologically (Putnam[21]).

Benedict's work seems further to be substantiated by Adler[1],

in whose series of 100 cases diagnosed as acute encephalitis of all varieties, fifteen per cent. eventually were recognized as multiple sclerosis because of the recurrence of attacks. Putnam has stated that certain types of encephalomyelitis represent the acute stage of a process which we know in its chronic relapsing form as multiple sclerosis. The "sheathing" of retinal blood vessels described by Rucker[22], and the studies of Franklin and Brickner[11] on vasospasm associated with multiple sclerosis appear to be two recent contributions to the study of multiple sclerosis which resemble similar pictures seen in the post-vaccinial ocular syndrome. There have been several cases observed following vaccination in which a process akin to "sheathing" has been seen in the fundus examination. An example of this type of ocular complication is the following: M.H., a 24-year-old male, was in apparently excellent health when he was re-vaccinated against smallpox. On awakening 21 days after vaccination he noted blurred vision more obtrusive in the right than in the left eye. Since he was unable to continue his clerical work, he consulted an ophthalmologist, who found the vision to be 20/50 in the right eye and 20/40 in the left eye. There was a mild bilateral macular oedema and a suggestion of general perivascular bifurcational constriction. The eye became worse in the next three days. Examined on the twenty-fourth post-vaccinial day, vision was 20/70 in each eye. At this time the macular oedema and perivascular sheathing were pronounced. Under vaso-dilators, atropine and rest there was gradual disappearance of the oedema, and return of vision to normal. Aetiological investigation revealed nothing abnormal. Franklin and Brickner in the above-mentioned paper have referred to the recent work of Zeligs'[28] in which macular oedema in young marines producing the characteristic "central serous retinopathy" is attributed to emotional tension with subsequent vasospasm. Franklin and Brickner state that "such tension has a profound and precipitating effect in cases of multiple sclerosis, as has been pointed out by several observers." I have listed five cases of the above syndrome, each coming on within a definite period following vaccination. Two of these cases were reported before the New York Society for Clinical Ophthalmology in May of 1947 and are summarized herein:—

Case 1—(*a*) Mr. M.C., a 38-year-old radio mechanic considered himself to be in good health. He had had no physical ailments for several years. There was no history of allergy either immediate or remote, nor of vasoneurosis, nervous tension nor other features associated with vasospasm. The patient did not smoke. On awakening three days after being vaccinated, he observed in front of his left eye a spot which was more noticeable when he gazed upon a white background.

Examination revealed a characteristic central serous retinopathic lesion. Physical examination including blood pressure studies were normal. The lesion cleared completely in three weeks. There was a central scotoma.

Case 2—(b) J.G., male jeweller aged 38 years, developed a spot before his left eye ten days after vaccination. The vision was only slightly impaired, so that he paid little attention to this impediment except when he attempted to use his jeweller's loupe. Then he found that he could not see an object unless he gazed at it eccentrically. When examined three weeks after vaccination, he was found to have a typical central serous retinitis, which cleared in three weeks. This patient had a mild hypertension. He has been under observation for the past twelve years and has hitherto never had any similar ocular condition.

The most dramatic cases in the post-vaccinial ocular syndrome are those of central serous retinopathy, for here the eye grounds reflect the process going on within the brain. Since post-vaccinial encephalitis has been shown to be limited to the vascular structures, and since central serous retinopathy is a condition in which the tiny macular twigs are involved with passage of fluid into the macula, it seems that in this region one can obtain a clue to certain phenomena arising in the brain. Since this area is vulnerable, the patient too will early be aware of involvement.

The classification of multiple sclerosis within the demyelinating diseases, the vascular distribution, the recognition of an hyper-allergic theory to account for the demyelinating diseases, and the unification of the pathology of the demyelinating diseases (Ferraro[6]) would seem to express a further relationship between post-vaccinial encephalitis and multiple sclerosis. Another case which shows at least a questionable relationship to multiple sclerosis is the following: L.D., adult male age 39, was re-vaccinated in May, 1947. Ten days after vaccination he developed an unsteadiness and a slight swaying to his left side. On the fourteenth day a small central scotoma was present in the right eye. He was found also to have an acute labyrinthitis. Symptoms cleared rapidly in four weeks. Upon neurological consultation he was advised that he might be suffering from acute multiple sclerosis.

In a recent experimental study Morrison[19] has produced encephalomyelitis in animals through the use of homologous antigen. He has speculated upon the possibility of a lipoid antigen resulting from demyelination which could produce such conditions as multiple sclerosis and other demyelinating diseases. His studies substantiate the work of Putnam and of Ferraro, who have repeatedly maintained that the type of lesion one sees in the demyelinating diseases depends to some extent at least on the age of the pathological process. Morrison emphasizes the similarity which exists between the demyelinating diseases and the pathological picture in his experimental encephalomyelitis, which reaction is based upon an immunological response.

Autopsy displayed definite arterial occlusion in some of the animals—a controversial point mentioned by Greenfield[13] and Grinker[29]. If medullation is of great importance in this immunological study, perhaps careful observation could be made upon patients who have medullated optic nerves visible ophthalmoscopically, and upon animals with a normal medullation in the fundi.

During the recent episode of mass vaccination in and about New York City, I observed many vaccinated patients and have had several physicians inform me of various complications following vaccination. There is no doubt that a great many symptoms which follow vaccination are "flare-ups" of dormant conditions. This apparent "light-up" of a so-called dormant condition was the most frequently observed of the ocular complications. Usually there was a healed choroidal lesion which appeared to spring into activity after vaccination. Variation in the onset of the symptoms can be explained by the location of the lesion, especially in respect of its proximity to the macula, and by the degree of exudation. The following cases exemplify this variety of ocular complication :—

Case 1—Miss P., age 23 years, was vaccinated on May 18 in routine fashion. On May 30 she noticed in front of her left eye several large opacities, which became much more pronounced in the bright sunlight, or when she looked at a white background. At first there was only a slight blur, but within three days vision was reduced to counting of fingers. The patient was admitted to the Newark Eye and Ear Infirmary, where all routine studies proved to be negative. These included Wassermann test, urine, Mantoux (1:1,000,000 to 1:10,000 dilution), sinus studies and chest X-ray. Past history revealed chicken-pox, measles and whooping cough, all before the age of five years and all mild in character. There were no complications of these illnesses. The patient had never had any serious diseases and this hospitalization was her first. There was no family history of allergy and the patient had never had any indications of allergic reactions. She was first vaccinated at the age of one, with a normal response. Examination of this girl's eyes disclosed vision of fingers only in the left eye. The pupil was widely dilated; there were many large scattered precipitates on the back of the cornea. The vitreous contained many large greyish opacities, some globular in shape, others resembling large strands. These vitreous opacities were especially thick in the region of, or just anterior to, a large yellowish grey choroiditic patch about three disc-diameters in size. This exudate was quite recent, with edges still not healed and still non-pigmented. Although it was difficult to see through the turbid vitreous, particularly in this region, yet this lesion could be seen just a little beyond an old upper nasal choroiditic patch heavily pigmented and completely healed. The disc appeared normal, although it could not be seen clearly.

Case 2—Mrs. R., age 29 years, was moderately myopic. She had had annual refractions by a well-known ophthalmologist in New York City. Vision had always been normal with her glasses. Physical examination performed after the birth of her second child and three months before the onset of her present eye complaint indicated that there were no abnormalities. About twenty days after an uneventful re-vaccination the patient complained of small spots in front of her left eye. These gradually became more pronounced, leading to further visual obscuration. In about three days the vision was reduced to fingers at four feet.

At the initial examination the left eye was seen to have a severe choroido-retinitis with many large and small corneal precipitates, a turbid vitreous and a large choroiditic patch of recent origin and extremely exudative, in the upper nasal

quadrant. A small haemorrhage was adjacent. Near this new lesion were several smaller old, pigmented choroiditic patches all crowded along the path of the same blood-vessel. Under atropine, compresses, vaso-dilators and rest no appreciable improvement was noted in the next few weeks. The systemic investigation showed no aetiological factor, the following laboratory studies being reported upon as within normal limits: (1) Blood Count, (2) Blood sedimentation rate, (3) Blood chemistry, (4) Urinalysis, (5) Mantoux test 1:1,000 dilution, (6) Wassermann and Kahn, (7) X-ray of chest.

This group of cases illustrating a "light-up" of previously existing conditions need not necessarily be restricted to the eye. During the period of vaccination referred to in the above paragraph, complications following vaccination were seen in all of the specialities. The symptomatology in these specialities has been as variegated as are the symptoms and signs in post-vaccinial encephalitis, and, as in post-vaccinial encephalitis, this variegation should be considered of importance. As in the ophthalmic complications, the important factor is the appearance of symptoms at a specific time interval, namely, seven to twelve days. Thus the appearance of complications elsewhere in the body after the same interval should be regarded with significance. If one only remembers that the patient has been vaccinated, and seven days later he blossoms forth with an ocular complication, then that ocular complication is a product of the vaccination. The nature of the ocular complication is of no importance, from the aetiological point of view. This same principle applies to diseases of other organs.

As mentioned previously, it has been shown that the pathological picture of post-vaccinial encephalitis and the encephalitis of the acute exanthamata are identical. Krieder[15], in experiments and in autopsy studies in measles, has shown a perivascular lesion consisting of a thrombus formation, which explains the nature of the lesion. The participation of the central nervous system in uncomplicated measles is almost constant. The cerebral symptoms of measles, such as the changing uneasy capricious disposition, etc., are seldom considered neurologically. A meningo-encephalitic reaction is frequently seen, but these symptoms vanish very rapidly and are only lightly regarded. Wohlwill[26] has uncovered many lesions of the central nervous system, although encephalitic symptoms were masked during the course of the measles pneumonia. These changes were found at autopsy studies on patients who died of measles pneumonia. It has also been shown that in many cases of post-vaccinial encephalitis the lungs showed bronchial pneumonia of a type similar to that of the measles pneumonia. Parker Heath[14], in reporting upon a case of measles encephalitis, described an ophthalmoscopic picture resembling embolism of the central retinal artery. Because of the significance of this case I am repeating the report in some detail:—

Clinical History.—J.P., a boy of Italian parentage, aged 6 years, had developed measles eleven days before admission. There was a rash, and then convalescence. Blindness developed on the eleventh day after the onset of measles.

Eye Examination.—Ophthalmoscopic examination showed in the right eye a distinct pallor of the nerve head, and a loss of capillary colour, without loss of substance. The most extraordinary picture was seen in the arteries, which were reduced to threads, and were carrying little or no blood. The veins were dark in colour, and reduced in calibre throughout, but relative to the arteries were engorged. The entire retina showed loss of transparency not associated with haemorrhage or exudation. The foveal reflex appeared a deep red, somewhat diffuse, through a more exaggerated overlying non-transparent retina. The left eye presented essentially the same picture. Appearances resembled bilateral embolism of the central arteries. On the seventh day the patient's eyes responded to light stimuli for a short interval. On the tenth day the child suddenly announced that he could see. The fundi showed more filling of the arteries.

Since the pathology of post-measles and post-vaccinial encephalitis have been shown to be identical, it may be assumed that the histopathological picture found in Von Herrenschwand's second case could possibly produce a variation of the fundus picture seen in Heath's case. Heath's patient revealed an eye condition which was bilateral, oedematous, transitory, reversible and in several other features characteristic of allergy. The fundus picture may have been modified by the pressure exerted by fluid in the tissue spaces. The arterial thinning was related to this extra-arterial pressure, whereas the intra-arterial pressure likewise was unusually low, since the systemic diastolic blood pressure was reported as 40 or less.

Heath, in his statement, "It is very unlikely that an opportunity will ever arise for an anatomical study of a similar case," probably would be very interested in the *post mortem* report of Von Herrenschwand's case number two. It appears that, although Heath does not claim an allergic basis for this case report, yet the stressing of localized oedema as the dominant sign points toward such a concept. Furthermore, it would appear that the acute retinal oedema and other vascular changes in the retina in Heath's case, and the retrobulbar picture in Von Herrenschwand's case may be similar in nature to the acute perivascular pathology of encephalitis, if we make proper anatomical allowances. The similarity of the ocular picture shown above lends more significance to many transitory ocular symptoms casually mentioned in measles encephalomyelitis. These symptoms should be considered more gravely since Ford[10] has shown that recovery from measles encephalomyelitis is not nearly as complete as we have believed, and that sequels may arise several years later.

It is the purpose of this paper to show that ocular complications developing within a specific period after vaccination are part of a post-vaccinial ocular syndrome. That such a relationship may

exist in other organs is also hinted at. It would seem, therefore, to be worth while to investigate the state of the host a little more intently before performing vaccination.

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THE TREATMENT OF HYPOPYON ULCER OF THE CORNEA

BY

E. H. CAMERON

EDINBURGH

THE problem of the infected corneal ulcer in miners has for many years been a serious one in Edinburgh and has been a cause of considerable loss of vision and working capacity. About forty thousand miners are employed in the Lothians and Fife, and the great majority of the eye injuries which occur among them are treated in the Eye Department of the Royal Infirmary. For

many years the number of cases of the so-called "hypopyon ulcer" did not vary much, the average number of admissions per year to the writer's department, the charge of which he assumed in 1932, being about seventy-five. This figure represents about one half of the total number, as the Eye Department is a double one. Under the term "hypopyon ulcer" are included all corneal abrasions which show infiltration at the site of the injury with an inflammatory reaction, whether actual hypopyon is present or not. Two-thirds of the cases were miners, the remaining third consisting of workmen from other occupations with, in addition, a small senile group. Many of the cases did badly in spite of the employment of all forms of treatment then in use. In 1931 Dr. J. R. Paterson had read a paper at the Annual Congress of the Ophthalmological Society of the United Kingdom in which he reviewed 223 cases of traumatic infected corneal ulcer in miners, 182 of which had been treated in the Royal Infirmary. He used the records of cases that had been examined by his father, the late Dr. J. V. Paterson, in connection with claims for compensation. Of the total number, eighteen eyes were lost and only thirty-three retained vision of over 6/12. In over fifty per cent., vision was reduced to less than 6/60. The average stay in hospital was 29·4 days. These were deplorable results, and when, in 1935, the W. H. Ross Foundation for the study of Prevention of Blindness was founded under the guidance of Dr. A. H. H. Sinclair, it was decided to try to improve matters, and work on the problem was begun in 1937. The bacteriological aspects of the problem were investigated by A. J. Rhodes working under Professor Mackie of the Bacteriology Department, but, although much valuable information was obtained, this work gave no help with regard to prognosis and treatment.

In 1939 experimental work on animals was begun by J. M. Robson and G. I. Scott, working under Professor A. J. Clark of the Pharmacology Department, and the results of their research suggested that one of the soluble sulphonamides, sodium sulphacetamide, which is very soluble and non-irritating, should be given a thorough clinical trial both in prevention and therapy. Colonel R. M. Dickson, the Director of the Ross Foundation, undertook to arrange for the preparation to be introduced as a first-aid treatment at the pit-head and in the ambulance-room, and the Ophthalmic Staff of the Royal Infirmary readily agreed to undertake the necessary clinical trials. The results of this work are embodied in a number of papers which have been collected in a volume recently published by the University of London Press entitled "The W. H. Ross Foundation (Scotland) for the study of prevention of blindness." To many ophthalmic surgeons interested in the subject this volume may not, however, be readily accessible, and a short article describing the progress made seems desirable.

With the willing help of the colliery officials the first-aid treatment in the ambulance-room at the pit-head has been reorganised, and the danger of the neglect of apparently trivial eye injuries is now well understood by the officials and the miners themselves. When an eye injury is reported, sodium sulphacetamide in 10 per cent. solution is used as drops, and the miner is directed to continue to attend until danger of the development of serious trouble seems over. Any doubtful case is referred to his own doctor.

It has been the practice for many years to admit all cases of corneal abrasion coming to the Infirmary if they show evidence of even slight infection. These cases are all potential "hypopyon ulcers" and experience has proved the great danger of relying on out-patient treatment. From 1942 till March 1947 when the writer relinquished his charge, sodium sulphacetamide was used in routine treatment and almost entirely replaced other drugs. After penicillin came into general use it was given to supplement sodium sulphacetamide, but only in the now rarely occurring obstinate cases. More extensive use of it was made by Dr. C. W. Graham, who is in charge of the sister department, and his conclusions are given on page 20 of the Ross Foundation volume mentioned above. Sodium sulphacetamide was first used in 30 per cent. solution with considerable success. Dr. H. M. Traquair suggested its use as a solid powder, and, as this proved non-irritating and most efficacious, the writer decided on the following scheme of treatment which is still the standard routine in the hands of his successor, Dr. J. R. Paterson. Atropine is given in the usual way two or three times a day, and the conjunctival sac is kept free from secretion by means of a simple lotion. Sodium sulphacetamide powder is applied by the sister-in-charge a number of times a day, even two-hourly if necessary, and during the night as well in severe cases. After lightly cocainising the eye she heaps some of the powder on the surface of the ulcer, using a small spoon or some other convenient instrument, and holds the lids apart until the powder has dissolved. The number of applications is diminished as improvement takes place, and in the end drops are substituted. The patient is not discharged until danger of further spread of the ulceration has ceased, and when he goes home he is directed to use atropine and sodium sulphacetamide drops during the remainder of his convalescence. Any other form of treatment is now rarely necessary, cauterisation, paracentesis, Saemisch section etc., being seldom indicated.

Since 1942 only two eyes have been lost, one case being a shepherd in a poor state of health, and the other an elderly woman. In 1946, which may be taken as typical of the present position, the last complete year of the writer's charge, thirty cases were admitted, twenty-one being miners. Six were from other occupations and three were

senile cases. Of the twenty-one miners only three spent more than three weeks in hospital, and eight were in the ward for less than ten days. As a follow-up system in the case of miners who have returned to work is difficult to operate, there are records of vision in most cases only on their discharge. Four had vision of less than 6/60, six of 6/36 or better, and nine of 6/18 or better. In two cases there was no record. No miner's eye has been lost since 1942, as compared with the ten per cent. lost in the series reviewed in 1931.

It will be seen that during the last six years a great improvement has been brought about. In fact the method of treatment that has been adopted has altered the whole outlook with regard to hypopyon ulcers. A great deal of visual loss has been prevented, and the freeing of hospital beds that would otherwise have been occupied for long periods has been a great gain. It is possible that improvement in sanitation and working conditions in the pits has played its part, but the way in which the miners live has not greatly changed. Any alteration in the varieties of organisms that infect the cornea, or in their virulence, is improbable. It will be noted that the number of cases from other occupations has diminished also, and in this connection it must be borne in mind that the same first-aid treatment as at the collieries is now used in many works and factories of the area served by the Royal Infirmary. The newer drugs too are used by the practitioner in his surgery, and in the treatment of most corneal abrasions in the hospital out-patient department, whether there is evidence of infection or not. The fact, too, that both practitioner and workmen are more alive to the dangers of slight injuries brings cases to hospital earlier than in past years. When all these points have been taken into account it remains true that we have now a simple and convenient method of treatment which makes success in dealing with the ordinary typical case of hypopyon ulcer practically certain. These cases are no longer regarded with the former dismay and apprehension. A few still do badly — those in older people, those whose admission has been delayed, those in which a deep infection of the cornea through a small puncture has taken place, and a few for no apparent reason. It has been found that, if the sodium sulphacetamide treatment fails to produce early and rapid improvement, penicillin and other forms of treatment are rarely of much more help.

I am indebted to Dr. A. H. H. Sinclair, Colonel R. M. Dickson, Dr. H. M. Traquair and the members of the Staff of the Eye Department of the Royal Infirmary for help in the preparation of this paper.

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MODERN VIEWS OF SURGERY OF THE CORNEA*

BY

Professor M. SOBHY BEY

CAIRO

THE aim of this communication is to summarize briefly the present trends in corneal surgery, noting some of my own ideas and preferences, rather than to bring to your notice any particular item or procedure with which you are not already familiar.

For instance, you all know, but it is worth reiterating that, for a foreign body embedded deep in the stroma of the cornea, a keratome should be introduced behind it in the anterior chamber before cutting down on the foreign body from the surface; this is in order to offer counter-pressure from behind, and to prevent the foreign body being pushed into the anterior chamber.

Ulcers of the cornea, whether primary or complicating ophthalmias, are nowadays generally treated by the anti-biotic drugs. The latter are used locally either in the form of solutions for frequent instillations, or in the form of pastes as ointments, or in strong solutions mixed with adrenaline to be used as sub-conjunctival injections (Sorsby) or in the treatment by ionisation (Sallmann). These methods can be used in combination with each other, and many of the drugs in use can be mixed together in one powder (sulphadrugs+penicillin+streptomycin). The systemic treatment *per os* or by parenteral injections is, as a rule, added to the above.

If in a certain case the anti-biotic treatment is not efficacious, then pasteurization of the base and edge of the ulcer can be carried out by a thermophore regulated by a thermometer at 158° F. (Shahan). For those who have a pyrometric electrode for use in detachment of the retina, I recommend that this be used in place of the thermophore for carrying out the pasteurization, taking care to shorten the time of its application, because diathermy is more penetrating than the ordinary heat.

In ulcus corneae, it is always an advantage to lower the intra-ocular pressure even if this is within the normal limits; this ensures better nourishment to the cornea, and that is why repeated paracentesis is of great help in intractable cases.

In hypopyon ulcers, Saemisch advised his corneal section at the base of the ulcer from edge to edge. On the same principle, Sondermann prefers trephining the base of the ulcer using an Elliot's trephine for the purpose. Lindner recommends Elliot's

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operation of sclero-corneal trephining in order to avoid perforation of the ulcer itself, with its unfavourable sequelae of anterior synechia and prolapse of the iris. Nowadays keratoplasty has proved to be successful in those cases of corneal ulceration which do not respond to ordinary treatment; by means of this operation the infected tissue surrounding the ulcer is removed by the corneal trephine, and the disc is replaced by another taken from a donor or a cadaver. Superficial or lamellar keratoplasty has also given good results when done at the place of the ulcer or to the side of it (Filatoff).

Partial staphyloma can be excised by an elliptical incision, the lips of which are stitched. This may be done at the same time as an anti-glaucomatous iridectomy or at a subsequent operation.

Total staphyloma, when excised, leaves a satisfactory movable stump which is to be preferred to that obtained by grafts of cartilage, plastic or other materials implanted after the excision of the globe. When applied in suitable cases, and if properly done, no danger is to be expected. A contact glass, the optical part of which bears a design of an iris similar to that of the fellow eye, will be a good camouflage to an eye the cornea of which looks bad or is disfigured.

Keratectomy becomes inevitable in cases of symblepharon covering the cornea (see the work of Castroviejo and others). Partial or total superficial lamellar keratoplasty in the hands of experienced operators must take the place of total keratectomy (Paufique and Sourdille).

For recurring pterygium a buccal mucous membrane graft should be placed at the edge of the limbus and concentric to it, with or without a lamellar corneal graft shaped to cover the denuded corneal area obtained after dissecting the head of the pterygium.

Conical cornea, if not suited to contact glasses, has to be handled surgically. Cauterisation, perforation and cicatrization of the apex of the cone of the cornea, previously recommended, is no longer an operative necessity. Perforating keratoplasty is the best solution if agreed upon between patient and surgeon. Lindner advocates a new procedure: he introduces a Bowman's needle into the anterior chamber and with it scarifies Descemet's membrane in the weakest and thinnest area of the cornea at the apex of the cone. As a result, the stroma corresponding to the scarified area imbibes fluid from the aqueous and becomes thickened. Later this is followed by cicatrisation and some degree of flattening.

In incised wounds or traumatic ruptures of the cornea, if complicated by incarceration of iris tissue, the prolapsed part should

be pulled out and cut, and the iris reposed after cleaning the wound. The same applies to wounds of the sclera near the limbus. Corneal and scleral wounds should be stitched edge to edge, using very fine silk thread (No. 0000, supplied by N. Dugast, Paris) and small extra sharp needles (supplied by Grieshaber of Schaffhausen, Switzerland). Perfect coaptation of the edges of corneal wounds is a necessity; otherwise irregular astigmatism will result, and there is no satisfactory means of correcting it. If the surgeon is not in possession of the above instruments, he will have to resort to complete or partial conjunctival covering, according to the extent of the wound. The following is a useful modification of the conjunctivo-plastic flap: a rectangular flap of conjunctiva is prepared, starting its dissection as high as possible in the upper fornix; the flap is then turned down like an apron, with its epithelial surface in contact with the anterior surface of the cornea; with any form of flap and without corneal sutures, the accurate coaptation of the edges of the wound is largely a matter of luck.

When there is actual loss of corneal tissue as a result of lacerated wounds, conjunctivo-plasty must be used, and in such cases the raw surface of the flap should be applied to the cornea.

Barraquer was kind enough to supply me with exceedingly fine silk threads that can hardly be seen (crude silk), and they are advisable for corneal sutures. In the Vienna clinics (*e.g.*, Lindner's), Japanese or Chinese hair is employed; horse-hair can also be used. Extra care should be taken in sterilizing the hairs in the autoclave.

If prolapse of the iris takes place after perforation of a corneal ulcer, and conservative treatment with mydriatics does not succeed in breaking the anterior synechia, the patient must be prepared for surgical intervention. When the perforation and prolapse are of small size, a conical probe is used to push the iris back from its adhesions to the perforated part in the cornea; if this manoeuvre proves unsuccessful, subconjunctival injection of adrenaline and atropine might break down the adhesion; if this also fails, the prolapsed piece of iris is caught by an iris hook or by a fine iris forceps, pulled out and cut with scissors; this is followed by reposition of iris and by subconjunctival injection of adrenaline and atropine to prevent further formation of an anterior synechia. Should the corneal perforation be big enough to allow the entry of an iris repositor, it is recommended that the operator should use this repositor instead of the conical probe. In any case, care must be taken not to injure the lens.

Fistula of the cornea is usually associated with secondary glaucoma although the continuous loss of aqueous, of course,

gives rise to hypotony. Binocular bandage, rest in bed, and miotics, should be given a trial before a decompression operation is done. It is usual in such cases to perform a broad iridectomy. The latter, however, gives rise to much spherical aberration and astigmatism while, if you add to this the fact that the central or paracentral part of the cornea is occupied by an adherent leucoma, it is easy to understand why the resultant vision is usually poor. A better procedure is that recommended, many decades ago, in the Vienna school: a corneal trephining (the size of the trephine depends upon the extent of the anterior synechia) is made so as to include the fistula in the disc, and the trephine is applied obliquely in such a way as to obtain an incomplete disc with a trap-door hinge (Sachs). The door should give direct access to the part of the iris pulled and stretched by the anterior synechia. The latter is caught by a forceps or a blunt iris hook and cut, the corneal disc being pulled forwards during this manoeuvre. The hinged disc is then reposed, and binocular bandaging, as a rule, is enough to ensure closure and cicatrization of the corneal wound made by the trephine.

In the modern conception of keratoplasty, the corneal trephine is applied vertically, the whole disc is cut away and replaced by another taken from a donor's eye. Anyhow, the operator can either free the anterior synechia and do the keratoplasty at a subsequent sitting, or perform both at the same sitting.

If my Egyptian colleagues wish to practise keratoplasty, I advise them to do their best to combat the anterior synechia so often met with in this country as a result of the innumerable external diseases and ophthalmias. The anterior synechia is the enemy of the transplant, which will never remain clear if connected with the iris tissue.

Many operators have proved that a successful keratoplasty is far superior to visual iridectomy in central leucomata, even if these leucomata are tattooed.

SUMMARY

At present, anti-biotic treatment applied locally or systemically against ophthalmia has made ulceration of cornea a rarity, and when ulcers do occur they are less liable to perforate. Sclero-corneal trephining, as recommended by Lindner, obviates iris prolapse and adherent leucomata in hypopyon ulcers when perforation is imminent. If the iris prolapses, it should be freed from the cornea, pulled out and cut, if the defect in the stroma of the cornea is of moderate size. The deficiency in the cornea can be replaced by conjunctivoplasty and keratoplasty. The

same procedure is to be adopted for wounds of the cornea, the edges of which should be sutured in accurate apposition in order to avoid subsequent irregular astigmatism. When an adherent leucoma is already present, one should proceed as recommended by Sachs of Vienna, *i.e.*, the cornea in front of the adherent iris is incised with a corneal trephine applied obliquely, so as to cut an incomplete disc attached by a pedicle; the iris is then freed from the cornea by pulling on the adherent part and cutting it; the corneal disc is finally reposed with or without the insertion of sutures. A deep perforating keratoplasty may be necessary later for optical reasons. When Lindner's method does not bring attenuation of the ectasia of conical cornea, deep perforating keratoplasty is applied. Ectatic irregularity on the anterior surface of the cornea should be corrected by partial or total staphylectomy, and a better cosmetic effect is obtained by fitting a contact glass (Jena glass—Zeiss) on the corneal part of which an appropriate iris pattern and pupil are drawn. This is preferable to excision of the globe and the wearing of an artificial eye.

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INJECTION OF THE RETINAL VASCULAR SYSTEM IN ENUCLEATED EYES*

BY

I. C. MICHAELSON *and* H. F. STEEDMAN†

GLASGOW

So far as we know, studies of the injected retinal vascular system in man and animals have been dependent on injections given into the heart, internal carotid or ophthalmic arteries when the globe is *in situ*. This method does not permit the study of the injected retinae of eyes enucleated because of pathological conditions. To overcome this the following technique has been devised whereby an injection of the retinal capillaries of the freshly enucleated eye may be obtained.

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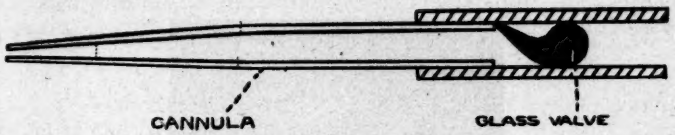
† From the Departments of Ophthalmology and Zoology, University of Glasgow.

Material and apparatus

A wash bottle or related container is used to hold the injection medium. It is supplied with air from a hand or foot pump, and is much more satisfactory than a syringe. The use of such a pressure bottle enables injections to be made in comfort and without an assistant. A Drechsel gas washing bottle is convenient. A mercury manometer should be incorporated in the system.

The outflow tube of the bottle is connected by rubber tubing to a cannula made by drawing out glass tubing.

An essential device in the apparatus is a glass valve in rubber tubing touching the cannula as shown in the following diagram.



Both the cannula and the valve are held between the finger and thumb so that when the cannula is inserted into the central retinal artery pressure of the thumb and finger allows the injection fluid to flow.

It is normal for erythrocytes to proceed through capillaries in single file and frequently under a certain degree of compression. It is therefore necessary that any suspension used for injection should have a particle size of less than 8 μ. It is also important that such particles should not flocculate, as otherwise both the cannula and the capillaries would become blocked. A material which is suitable for an injection of this type is Monastral Fast Blue, BVS paste produced by the Imperial Chemical Industries. The pigment paste should be diluted with water in the ratio of three parts water to one part paste. Indian ink was also found to be suitable.

In the freshly enucleated eye it is impossible to insert the cannula into the central retinal artery because the optic nerve is so soft that it moves away from the cannula. A certain amount of fixation is therefore necessary before attempting the injection. The pressure in the apparatus must clearly exceed the intra-ocular pressure and in practice a considerable excess of pressure is an advantage. The most desirable pressure is that which will give the fastest injection with the least chance of bursting the capillaries. In this connection the pressure, the bore of the cannula and the viscosity of the injection fluid are all related. For the sake of convenience the relevant figures follow in table form.

Glass tubing for cannula, ext. diam.	3	mm.
Glass tubing for cannula, bore	1	mm.
Cannula point, ext. diam.	270	microns.
Cannula point, bore	90	microns.
Injection pressure	300	mm. mercury.
Injection time	5–15	seconds.
Room temperature	65°	F.

Method

1. Fix the fresh eye in 5 per cent. formol for 30 minutes to two hours.
2. Wash in tap water 10-30 minutes.
3. Arrange the eye in a plasticine ring optic nerve uppermost, on the stage of a binocular microscope. Eyepiece x6, objective 49 mm.

4. Cut a thin slice from the end of the optic nerve so that a new, smooth surface is exposed.
5. Insert the cannula into the artery or vein and inject.
6. Place the globe in 10 per cent. formol for 24-48 hours.

Results

Although the injection is not successful in all cases the results generally are satisfactory. After the second fixation is complete the globe is bisected coronally about the region of the ora serrata

FIG 1.

and the vitreous is gently swabbed from the posterior portion. This portion is then mounted in a special holder and examined with the slit-lamp. As an example of the appearances which may be obtained in this way, Fig. 1 illustrates an injected rete mirabile

FIG. 2.

Portion of mounted retina of human eye injected after enucleation showing normal vascular system.

lying in front of the optic disc in a case of venous obstruction. The retina is subsequently peeled away from the choroidal bed and mounted on a slide in glycerine. The appearance of a portion of injected retina mounted in the manner described is illustrated in Fig. 2.

This method of examining the retinal vascular system would appear to open new possibilities in the investigation of various fundal states including the relationship between the colour of the optic disc and its capillary content, the state of the capillary bed especially at the edge of the disc in glaucoma, and its relationship to visual field defects, new-vessel formation in the retina and vitreous, the extent of the capillary free zone at the macula in various conditions, etc.

It also affords an opportunity of investigating the degree of collateral circulation existing in the optic nerve head and choroid.

Summary

1. A method is described of injecting the retinal vascular system in the freshly enucleated eye.

2. Indication is given of the possible usefulness of this new technique.

SEVERE LESION OF THE VISUAL PATH IN PREGNANCY*

BY

G. PERÉMY

BUDAPEST

RECENTLY I had the opportunity to review the condition of a patient whom I saw for the first time nearly 20 years ago. The case seems to be a very rare one. The case described by Lawford Knaggs more than half a century ago is closely similar to the one I am going to relate, but in the literature of the last years, as far as I had access to it, I could not trace another of that kind.

Case history.—The patient was sent in 1930 by the ophthalmologist to the First Medical Clinic of the University of Budapest for consultation on account of the rapid deterioration of the vision of her left eye. She was at that time 40 years of age and in the fourth month of her sixth pregnancy. She had already gone through three pregnancies when she accidentally became aware of the complete loss of the vision of her right eye. This happened six years earlier. In her earlier history there was nothing which could have been brought into relationship with her condition at that time, except for an apparently insignificant, slight headache which she had sometimes since her 'teens. The medical examination revealed a normal physical condition, including blood-pressure, urine and blood picture. The Wassermann test was negative. The ophthalmological data were as follows: The right pupil reacted to light only consensually, the left one only directly. Amaurosis and primary optic atrophy were found in the right eye. With the left eye she could count fingers at seven feet. The margin of the left optic disc was sharp,

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and it was somewhat reddish, no papilloedema was to be observed. There was a complete central scotoma for all colours, the visual field was contracted in a high degree for red, less for white. The patient had a marked squint as a result of the amaurosis. Examination of the nervous system revealed no abnormalities. The senses of smell and taste were also normal. The pressure and the composition of the cerebrospinal fluid were normal. X-ray plates of the skull showed no signs of increased intracranial pressure. The size and the shape of the sella turcica were normal. The sinuses were clear.

The optic atrophy on the one side and the retrobulbar neuritis on the other were judged to be caused by the pregnancies. The interruption of the pregnancy of the time seemed inevitable, yet the patient left the clinic and induction was not performed until one month later, after further deterioration of her vision. I asked her to come to the clinic for re-examination. She did so two and a half years later. She said she had experienced an improvement of her vision for some months after the interruption of her pregnancy, and since then it was unchanged. She had still her menstrual flow regularly. She had no complaints. A complete loss of the temporal half of the left visual field was found. The perception of red and green in the centre of the nasal half was retained. On being asked, she related that for some time she was forced to turn her head excessively to the left when crossing a street, or else she was unaware of vehicles coming from that side. An X-ray plate of the sella showed it to be unaltered. She had put on some weight, but there were no signs of abnormalities of nervous or hypophyseal origin. The urine and the blood-pressure were normal. The findings of the ophthalmologist were as follows: The condition of the right eye was the same as at the examination two and a half years earlier. The vision of the left eye was 5/10. The left optic disc was pale. There was a temporal hemianopia. The nasal colour-fields were normal.

On re-examining the patient some weeks ago, I found that her ophthalmological condition remained unchanged. In particular the nasal colour-fields were intact. Neither could I find any other change in the condition of the patient.

There could be no doubt that this severe lesion of the visual path had been brought about by pregnancies. It could have been caused by toxic damage to the optic fibres, or by pregnancy-enlargement of the adenohypophysis, though both possibilities were equally hypothetical. The later ophthalmological findings revealed a damage to the optic chiasma or to the right optic tract too (the right eye already being amaurotic). On the basis of this condition I suggested that there might have been some benign cystic growth of the hypophysis which exerted a pressure on the chiasma mediated through the pregnancy-enlargement of the adenohypophysis. But the course of the disease and the present condition of the patient make such a hypothesis extremely unlikely. Certainly signs of increased intracranial pressure were never observed, and no change in the size and shape of the sella occurred. Neither did any other nervous or endocrine disorder develop. In a case of such a strong and repeatedly exerted pressure on the visual path which resulted in the atrophy of one optic nerve and one optic tract, other signs too should be expected, *e.g.*, a disturbance of smell, and the cardinal signs of hypophyseal-diencephalic hypofunction. Yet no sign of that kind appeared in more than 20 years. Thus we are led to assume repeated toxic damage to the optic fibres resulting from pregnancy, which first brought about a complete atrophy of one optic nerve, and later

affected the remaining fibres of one optic tract too. Toxic damage to the optic fibres including that which is associated with pregnancy is exerted in most cases on the retrobulbar part of the axial fibres of the optic nerve, and thus arises what is known as retrobulbar neuritis. The damage to the optic fibres originating in the left retina of the patient was initiated in this way. This may support the assumption of a toxic origin, though the impairment of central vision may also be an early sign of pressure. The peculiar feature of the case presented here is that the toxic damage should extend so far along the visual path. The multiplicity of pregnancies may account for this. In such cases the task of differentiating a toxic state from that caused by a tumour in or near the sella may arise. As I tried to show, the hemianopic defect of the visual field does not prove beyond doubt that it is caused by the pressure of a neoplasm; it may be the result of the same toxic damage to the optic tract as that which affected the optic nerve. Cases may occur in which the alternative—pressure or toxic damage—cannot be decided for a while. Decision may sometimes be possible only in the later course of the disease. Fortunately in cases of pregnancy such uncertainty does not imply any therapeutical dilemma, since termination of the pregnancy is warranted in the case of an alleged tumour especially if the impairment of vision seems severe; and it is known that the growth of a hypophyseal adenoma may be stimulated by simultaneous pregnancy.

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AN UNUSUAL CONGENITAL DEFECT*

BY

ALLAN H. BRIGGS *and* D. W. MCLEAN

LINCOLN FOLKESTONE

DAPHNE S. was brought to one of us (A.H.B.) at the age of fourteen days, as the parents had noticed an abnormality of the right eye since birth. The child was normal and healthy in all other respects, and there was no family history of known ophthalmic defect. The pregnancy and labour were apparently normal.

On examination, difficult in so small an infant, it was found that the lids and adnexa were normal. The eye was white and of

* Received for publication, November 16, 1948.

normal dimensions. The cornea was clear and bright with no precipitates, but in the upper inner quadrant a pink fleshy mass was present in the anterior chamber, touching and apparently adhering to the posterior corneal surface, and occupying the whole depth of the anterior chamber in this area.

The mass was rounded and apparently solid in nature, and appeared to spring from the region of the root of the iris. It was

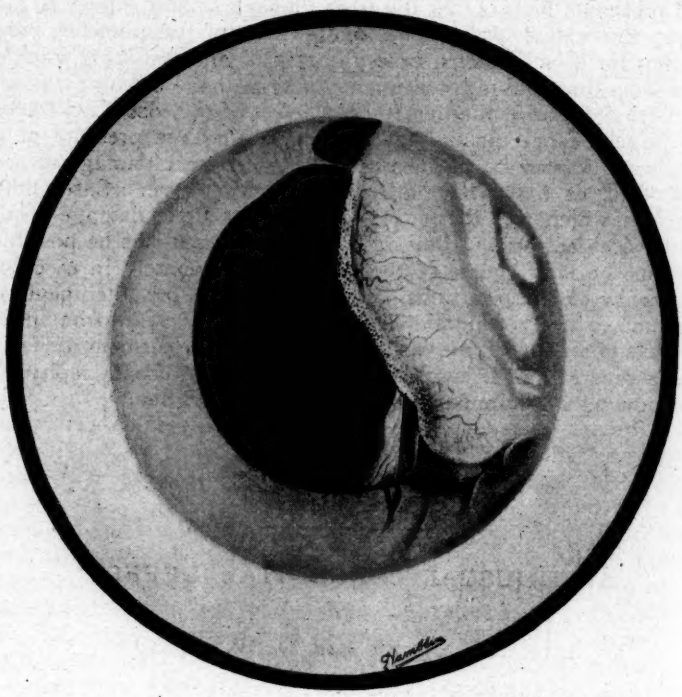

FIG. 1.

approximately 3 mm. in diameter. The anterior chamber was clear and of normal depth. The iris was normal except that there was a coloboma in the area occupied by the tumour, its margins attached to the tumour by multiple fine vascular strands. The lens was mainly clear, but with a slight posterior opacity, and there was evidence of vascular strands still present in the anterior part of the vitreous. Very little view could be obtained of the fundus,

even when the pupil was dilated with atropine, but no gross abnormality was discovered.

The child was kept under observation, and in two months it was found that the tumour was not quite so solid in appearance, and vessels could be made out on its surface. It was possible to do an approximate refraction, which showed a high degree of irregular astigmatism.

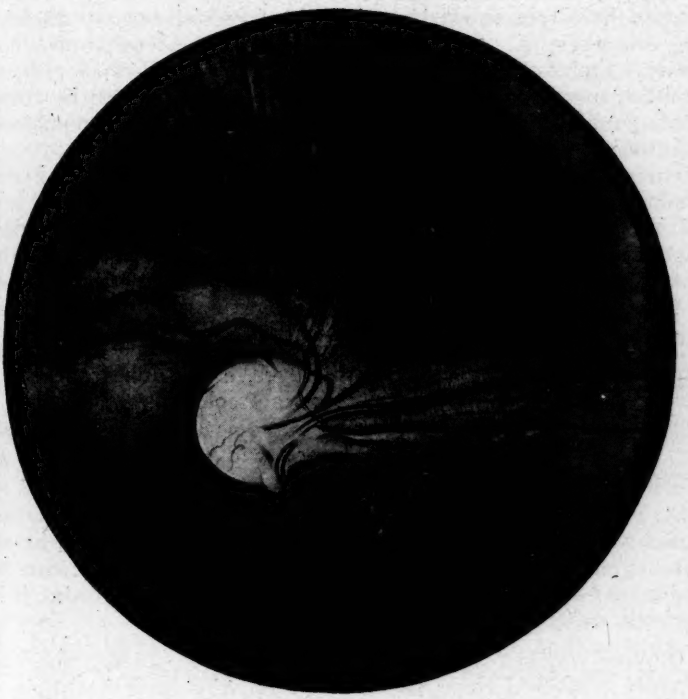

FIG. 2.

At the age of four months the condition had undergone no evident change, and further examinations at nine months and sixteen months revealed very little alteration in size or appearance.

Daphne then removed with her parents and was seen (by D.W.M.) in April, 1948, at the age of nearly six years. The occasion was the development of a right convergent squint three months earlier, following a mastoiditis which resolved without

operation. Under atropine the refraction of the right eye showed a large and irregular myopic astigmatism, and even with correction there was little useful vision. The left eye had three dioptres of hypermetropia, its vision was full and its fundus healthy.

The right eye showed a large iris coloboma on the nasal side which was completely filled by a rounded pink mass with fine vessels running over its surface. This mass extended almost half way across the dilated pupil, and protruded into the anterior chamber so as almost to touch the cornea. Over the base of the tumour the cornea showed two islands of greyish opacity resembling arcus senilis. The eye was white, and the tension was not raised. Ophthalmoscopy revealed thin strands of persistent pupillary membrane, and at the lower pole of the tumour the fibres of the zonular ligament were exposed. There was an anomalous distribution of vessels at the optic disc.

The patient's mother was able to give a detailed history of the condition, but she said that, a year earlier, a doctor had told her that the vision of the right eye was normal. Though this seemed improbable, a slight doubt was raised whether, after all, the condition were as static as it appeared, and in view of this the opinion of Miss Ida Mann was obtained. She commented (June, 1948):—

"The condition is a most unusual one and I have never seen anything quite like it. It has, however, every appearance of a congenital abnormality in that there is a coloboma of the iris, a *situs inversus* of the disc, a very high myopic astigmatism, a small tag of persistent pupillary membrane, and complete absence of inflammatory reaction or raised tension.

"... I am strongly of opinion that nothing should be done. I would suggest, however, that an accurate painting be made by an ophthalmic artist, which could be used for comparison six months and a year hence. If there is no change in that time I think it is perfectly safe to leave the eye alone."

Daphne was last seen (D.W.M.) in October, 1948. She had recently recovered from mumps, was in very good health, and though her strabismus was pronounced there was no discoverable alteration in the picture of her right eye.

The writers wish to express their appreciation of Miss Mann's courtesy in permitting them to quote excerpts from her letter.

A CASE OF OCULAR MYIASIS

BY

E. E. CASS

GIBRALTAR

OCULAR myiasis is rarely seen in Western Europe. It usually occurs in hot countries, where there are many flies, and the living and sanitary conditions are bad, and the people dirty and ill-nourished.

The most common fly which causes myiasis belongs to the muscoid group, amongst which the common house fly is the most usual cause of the trouble; all of this group lay eggs, usually choosing filthy situations, such as manure heaps, decomposing flesh, festering wounds, and sometimes the lids of people who are in a debilitated filthy state, with discharging eyes. If these flies do lay their eggs in the conjunctival sac, the majority lay them on the surface of the conjunctiva, but some are more dangerous, as their maggots burrow below the conjunctiva and penetrate the globe.

The oestridae possess ovipositors, and can lay their eggs beneath the conjunctiva itself, and one of them, the hypoderma bovis, can penetrate the globe. Luckily such cases of intra-ocular myiasis are very rare.

The sarcophagidae and anthomydae can also infect the conjunctiva of man.

The severity of the condition depends on the type of insect which has laid its egg in the eye, the condition of the patient, and, naturally, the longer the patient is left without treatment, the more severe is the reaction in the eye.

In the milder cases there is usually the history of a fly having entered the eye and being removed, but the discomfort does not diminish; there is increasing pain, lacrimation, and swelling of the lids and conjunctiva, and on examination the maggots are seen crawling in the eye. With removal of all the maggots the condition subsides. In the filthy ill-nourished patients who do not receive treatment, with numerous maggots, the larvae may hatch out and the whole eye be destroyed by the flies, and the orbit itself invaded, with consequent meningitis and death.

In cases of intra-ocular myiasis, intense pain and other symptoms of iritis are present. The parasite can be removed if it is in the anterior chamber, with some conservation of vision, but if it is in the retina, enucleation has to be performed. 32 such cases have been described, of which 21 occurred in the anterior chamber. In

the past 18 months 3 cases have been described in the Archivos de la Sociedad Oftalmologica Hispano-Americana; in two, larval conjunctivitis occurred, and in one of these, the patient had pre-existing trachoma. Removal of the parasites resulted in relief of the symptoms. The third case was that of an intra-ocular myiasis caused by hypoderma bovis. Removal from the angle of the A.C. of a mass, containing the parasites, resulted in relief of pain and a rapid subsidence of ocular signs and gradual return of normal vision.

The only case which has been recorded in Gibraltar is as follows: a healthy male Spaniard of 35 years was passing near a cement mixer, when he complained that some of the dust blew into his eye. A friend washed out his eye with water from a nearby tap. This occurred at 5 p.m., and the eye was immediately painful. By 10 p.m. he was suffering from intense pain, and could not sleep. His wife looked in his eye, and removed two small white bodies from it, but the pain still persisted. On the following morning he came to the Colonial Hospital, Gibraltar, sent up as a "cement burn" and immediately had his eye washed out. The nurse appeared in great agitation, saying that the man had "some white things walking in his eye." On examination he had swelling of the lids, with blepharo-spasm, pain and photophobia. The conjunctiva was oedematous and very inflamed. One small maggot, about 2 mm. long, was seen walking across the cornea, and was removed with a rod. It was pear shaped and, with the loupe, a depression was seen on the under surface of the head together with tiny suckers. The head of another maggot was seen emerging from a burrow in the conjunctiva. Cocaine 5 per cent. was inserted, and seven maggots were removed with a needle, and sent to the laboratory for identification.

The eye was irrigated with hyd. perchlor. (1:10,000), and the patient was left to wait for an hour, and then examined again. Another maggot was then removed: this had burrowed into the conjunctiva and had to be levered out.

The patient again was examined after another hour, but no further maggots were found, so the eye was irrigated, oil inserted, a flap applied, and he was allowed to return home. The next day the eye was still injected in the lower fornix, and was still slightly painful, but no more larvae were found. He was ordered irrigations and oil. Two days later there was no pain, and only slight injection below.

In this case 11 maggots in all were found. The greatest number reported in larval conjunctivitis has been 77.

The man was seeking compensation, and insisted that no fly had been in his eye, but that the maggots must have been in the cement mixture, or the tap-water. The larvae were identified as those of Phlebotonus (sand-fly) and both cement and the tap water were examined for larvae with negative result.

It is probable that the small fly entered his eye with the dust, and was not seen by the friend who washed out the eye.

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THE LACRIMAL STRIP AND THE PRECORNEAL FILM IN CASES OF SJÖGREN'S SYNDROME

BY

M. KLEIN

LONDON

WOLFF has recently suggested that the precorneal film has a triple structure, consisting of a deep mucoid layer, an intermediate lacrimal watery layer, and an oily layer which is very thin (probably not more than of monomolecular thickness), and which floats on the surface of the lacrimal layer.[1,2] This composite film is the product of different glands and of a mechanism to maintain it. The mucous layer derives from the goblet cells of the conjunctiva, the watery layer from the main and accessory lacrimal glands, and the oily layer from the tarsal glands. The precorneal film is maintained by the following mechanism: Whenever the eye is closed the palpebral conjunctiva comes into direct contact with the cornea, and the mucus from the goblet cells is spread over its surface. The lacrimal layer is responsible for the brightness of the corneal surface, and being completely transparent normally it cannot be seen, but after the instillation of fluorescein it shows up clearly even to the naked eye. An accumulation of this watery layer, the marginal strips, can be easily seen in the gutter formed by the lid margins touching the globe. With every descent of the lid this lacrimal strip replenishes and maintains the watery film. Apart from these anatomical and mechanical factors the relatively high protein content of the tears contributes to the evenness and stability of the lacrimal layer. The oily film can best be seen by the slit-lamp, the beam being directed on the free lid margin and the cornea illuminated by the reflected light.[3] Sometimes one can see the oily layer even with the naked eye as coloured rings, or as a fine membrane with polychromatic lustre.

It was of interest to observe the lacrimal strip and the precorneal film in several cases of keratoconjunctivitis sicca. Sjögren described how the conjunctiva and cornea lose their brightness, although as a rule they do not look dry. Though in all our observed cases Schirmer's test indicated very marked reduction in, or almost absence of lacrimal secretion, the marginal strips of tear fluid were present in all cases. The precorneal film lacked the easy-flowing flexible appearance of the normal film and was rather viscous. The oily superficial layer was also present.

Though we are dealing with keratoconjunctivitis sicca, the

* Received for publication, September 13, 1948.

marginal strips of tear fluid and the precorneal film are present, a point which so far as I am aware has not been made. Moreover the precorneal film seems to be composed of the usual three elements, but the mucoid component apparently predominates over the lacrimal film. Whether this is due to diminished lacrimal secretion alone, or the composition of the tear fluid is altered as well, needs further investigation. According to Frederick Ridley the protein content of the tears is reduced in cases of Sjögren's syndrome and in xerosis (personal communication). This may be significant, as the surface tension of the tears is influenced by the protein content, and with it the quality of the precorneal film.

My thanks are due to Mr. Eugene Wolff in whose clinic at the Royal Westminster Eye Hospital these observations were carried out, for his interest and helpful suggestions.

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THE RELATION BETWEEN PERIPHERAL RETINAL CYSTS AND DIALYSES*

BY

SIR STEWART DUKE-ELDER

LONDON

THE simultaneous occurrence of cysts at the periphery of the retina and dialyses has been remarked on several occasions, and although a close relation between the two has been suggested, I have been unable to find definite proof that a dialysis may develop from the bursting of a cyst. The following case, which by a fortunate chance illustrated this sequence, is therefore of importance.

A healthy adult male, aged 44 years, was first seen on April 16, 1946; distant vision was normal and his only complaint was of presbyopia. In the left eye, however, a typical retinal cyst, approximately 2 × 1 disc diam., occupied the extreme periphery in the usual position, down and out at about 5 o'clock. He was seen three months later, when the cyst showed no observable change. After a further three months, however, the cyst had enlarged by about one-third and, although he had no subjective symptoms, in view of the fact that he proposed to go abroad for some years, an operation was arranged, the intention being to puncture the cyst by

* Received for publication, February 14, 1949.

diathermy. He was seen again on December 2, 1946, the evening before operation, when the cyst was found to be more than double its original size. The next day, immediately before operation, a final ophthalmoscopic examination was made, and in place of the cyst a dialysis was seen occupying an area exactly corresponding to that previously occupied by the cyst, associated with a shallow detachment of the retina running a considerable way towards the disc. Diathermic coagulation was performed with a satisfactory result; six months later the retina was completely re-apposed and the vision was 6/5.

FACULTY OF OPHTHALMOLOGISTS

The following is the Honorary Secretary's summary of the business conducted at the last Council meeting on April 29:—

The following were elected Officers for 1949-50:—

President: Mr. Frank W. Law; *Vice-President:* Mr. J. J. Healy; *Honorary Secretary:* Mr. J. H. Doggart; *Honorary Treasurer:* Mr. A. B. Nutt.

It was reported that Dr. Charles Hill had written to the Ministry of Health protesting against the reduction in fee for work under the Supplementary Ophthalmic Service. It was also reported that a letter had been received from the Ministry of Health, stating that Mr. W. Penman was willing to undertake an investigation of the average time taken for a sight-test, and asking the Faculty to nominate four members to be associated with him as an informal working party to watch the investigation and study the results. Mr. Black, Mr. Healy, Mr. Gayer Morgan and Mr. Simpson have been nominated to represent both the Ophthalmic Group Committee of the British Medical Association and the Faculty.

It was learnt that the practice of referring patients from the hospital clinics to the Supplementary Ophthalmic Service did not meet with the approval of the authorities. It was agreed to write to the Ministry stating that the Faculty did not approve of this practice, but until more assistance, technically and financially, was received towards the progress of the Permanent Service there did not appear to be any alternative. It was also decided to point out that the prescriptions of the patients seen in Hospital must be made up in the Hospital; otherwise there would be no saving financially.

The draft handbook for ophthalmic medical practitioners and ophthalmic opticians, together with the comments of the Ophthalmic Group Committee, was considered. The Ophthalmic Group Committee's comments were approved, but it was felt that it should

be illegal for an optician to prescribe glasses for any case which had been referred back to the general practitioner. It was decided to recommend to the Ophthalmic Group Committee that representatives from the Committee and the Faculty should discuss this point with the Ministry, and the Chairman of the Group Committee and Mr. Law were nominated to act in this capacity.

At the suggestion of the Ministry of Health a Committee of Referees is to be set up to deal with matters arising from the regulations governing the working of the Supplementary Ophthalmic Service.

A letter was received enquiring whether a spare pair of glasses should be issued to cover the risk of breakage. It was reported that this had been referred to the Ministry of Health, who had replied that under the Supplementary Ophthalmic Service and the Hospital Eye Service a patient was not entitled to glasses if already in possession of a pair.

It was reported that a letter received from a member regarding domiciliary visits had been referred to the Ministry of Health, who had replied that if the Supplementary Service was used for bedridden patients the ophthalmic medical practitioner or ophthalmic optician could, if he wished, ask the patient for a reasonable fee for visiting him instead of the patient attending his consulting rooms. The Ministry felt, however, that all bedridden cases should be brought under the Hospital Eye Service and not the Supplementary Service.

It was agreed to call a meeting, consisting of the Officers of the Faculty and the Ophthalmic Advisors to the Regional Hospital Boards, to consider points in connection with the Permanent Service.

It was learnt that, in spite of protests from the Faculty, the Ministry of Labour and National Service had decided to reduce the fee payable to ophthalmic medical practitioners for sight tests made on and after April 1st, 1949, under the National Health Service from £1.11s.6d. to £1.5s.0d.

A request from the Joint Committee for Consultants to draw up criteria for consultants and specialists for the specific purpose of assisting those considering appeals from the decisions of the Review Committees was considered. After discussion, it was agreed to submit the following recommendations:—

1. Consultants should have ten years' approved training and experience in ophthalmology in all its branches after qualification.

2. Consultants must hold a higher degree or diploma.

3. Consultants must hold or have held a recognised appointment to a hospital.

A letter was read from the Ministry of Health giving the terms of reference and constitution of the proposed Committee on the

registration of opticians. The suggested terms of reference were "on the assumption that it would be to the public interest that provision should be made by legislation for the registration of opticians, to advise how registration could best be carried out, and what qualifications should be required as a condition of registration." The Ministry suggested that the Committee should consist of twelve members under a lay chairman to be appointed by the Minister, the members consisting of 3 ophthalmologists (1 from Scotland), 1 physician, 1 physiologist — 4 ophthalmic opticians (1 from Scotland), 1 dispensing optician — 1 physicist and 1 Member of Parliament (neither medical nor optical). The Faculty was asked to submit nominations for the first group. Though it was felt that ophthalmology was not adequately represented, it was agreed to submit nominations jointly with the Ophthalmic Group Committee of the B.M.A.

The recommendations made by the Joint Advisory Board of the Optical Profession to the Examining Bodies on the training and examination of future entrants to the optical profession were considered. It was decided:—

(*a*) That the General Anatomy and Physiology section was too detailed.

(*b*) To ask for further information regarding the examination in the use of drugs.

(*c*) That the section dealing with Abnormal Ocular Conditions in the syllabus and in the examination should be deleted. It was agreed that opticians who worked in hospitals would have an opportunity for practical experience in recognising diseases, but that this should not form part of the qualifying examination.

The question of lecturing to opticians again arose. Although the Council felt that there was no objection to members giving an occasional lecture on an optical or medico-political subject, it was agreed that a final decision could not be made until the report had been received from the Commission on the registration of opticians.

A memorandum on the practice of orthoptics has been prepared and will shortly be published in the British Medical Journal.

Regarding the proposed changes in the system of the training of nurses, it was decided to ask Mr. Law to approach the ophthalmic matrons to enquire what action had been taken, and to raise the matter with the Royal College of Nursing.

It was realised that the Regional representation on the Council left something to be desired, and letters pointing this out had been received by the Honorary Secretary. It was finally decided to alter the regions to correspond with those defined under the National Health Service. The Council will be reconstituted as follows:—

(*a*) One Member elected from each Region under the National Health Service (14).

(*b*) One Member from Scotland.

(*c*) One Member from Northern Ireland.

(*d*) One National representative from the Full and Part-time Associates.

(*e*) Eight National Member representatives.

Such an arrangement would leave its total number unchanged.

BOOK NOTICES

The Management of Binocular Imbalance. By E. KRIMSKY (New York). 464 pages, 200 figs. Henry Kimpton (London), 1948. Price 63/-.

A number of books on the ocular muscles and the problems of their imbalance have appeared in recent years, but this volume has the very considerable merits of being at once interesting and stimulating. It takes as its text the corneal reflex, and shows how this can be exploited by means of the simple equipment of a flash-light and prism to form the basis of an extremely complete objective and subjective analysis of the binocular function and state of motility. The corneal light reflex has, of course, been employed for many years by such investigators as Hirschberg, v. Graefe, Priestley Smith, Tscherning, Landolt and innumerable others in the investigation of squint, but no one has yet attempted so thorough an exploitation of its potentialities as to include not only an examination of monocular and binocular fixation, the angle of latent and manifest deviation in squint, but also, among other things, the measurement of the depth and area of suppression in a deviating eye, the elicitation and location of abnormal correspondences and false projection, the proof of the existence of diplopia and the analysis of head-tilt. The theory of the method is well-known: the corneal "reflex" is an erect virtual image formed behind the cornea which in the normally fixing eye occupies a "neutral" position centrally (apart from the angle gamma) in the pupillary area; on the displacement of the eye out of the normal position of fixation, the reflex is also displaced, and can be restored to the neutral position by placing the appropriate prism in the required position in front of the cornea. Latent deviation can similarly be estimated by dissociating the two eyes with a prism

acting at right angles to the direction of ocular deviation and again restoring the corneal reflex to a symmetrical position. By exploiting to the full these elementary principles with the aid of the simplest apparatus the author has built up a most comprehensive and thought-provoking treatment of his subject.

Everyone will not agree with him on all his conclusions, such as the valuelessness—or sometimes the dangers—of total occlusion. He himself has strictures to make upon such matters as the value of the existing tests in Air-Force examinations and screening tests for industrial workers, all of which are of interest. On the whole the book—which is excellently produced—is of considerable value and worth study.

Dermatologie für Augenärzte. (Dermatology for the Ophthalmologist). W. SCHÖNFELD. Pp. 109., 47 figs, 45 colour plates. G. Thieme Verlag (Stuttgart), 1947.

This is a very useful contribution to ophthalmic literature, for the diseases of the skin which have an ophthalmological bearing and present problems, frequently of considerable difficulty to the ophthalmologist, are many. The first part of the book gives a concise and clear discussion on the three main diatheses which influence the incidence of such diseases — the seborrhoeic, the exudative (scrofulous) and the allergic; there follows a description of the techniques of skin tests and a review of general information regarding the various types of medicaments used therapeutically (lotions, ointments, pastes, etc.). The remainder of the book describes in a systematic way the various skin diseases which may affect the lids, including neoplastic conditions and affections of the brows, lashes and associated glands. The writing is clear, the clinical photographs good, and the atlas of coloured illustrations at the end of the book excellent.

Einführung in die Augenheilkunde. (Introduction to Ophthalmology). P. A. JAENSCH. Pp. 228, 185 figs. G. Thieme Verlag (Stuttgart), 1947.

This elementaty text-book of ophthalmology suitable for the general student has much to recommend it. It is small and compact, clearly written, well illustrated and confines itself to the essentials of the subject. The usual systematic arrangement is adopted — a description of the anatomy, physiology (including optics) and embryology of the visual apparatus is followed by a systematic discussion of the pathological conditions affecting the eye and its adnexa, particular attention being paid to the aspects of ophthalmology which impinge on general medicine. For its intended audience the book is good.

OBITUARY

FRANK GRIFFITH THOMAS

WE regret to have to record the death of Frank Griffith Thomas, aged 76 years, on March 22, at Bournemouth, where he had recently been living in retirement.

His passing removes another link with the pioneers of provincial ophthalmology, for his father, Dr. Jabez Thomas of Swansea was one of those medical practitioners, who during the latter part of the 19th century, by reason of a clinical flair allied to wide knowledge and force of character, gradually assumed the rôle of consultant in provincial towns. Jabez Thomas devoted much of his time to the study and treatment of eye diseases, and eventually was responsible for the opening of an eye department at the Swansea General Hospital.

Frank Thomas received his scientific and early medical training at Cambridge where he graduated B.A. (National Science Tripos) in 1893. He finished his training at Guy's Hospital where after graduating M.B. B.S. in 1897 he became House Physician and Clinical Assistant. Concentrating on ophthalmology, he acted as a Clinical Assistant at Moorfields, and later became Registrar at the Royal Eye Hospital before returning to Swansea in 1900, where he succeeded his father as Honorary Ophthalmic Surgeon to the Swansea General and Eye Hospital. He shortly afterwards married Dr. Florence Margaret, daughter of the late Dr. Price of Carmarthen, and herself an ophthalmologist, who assisted her husband in his work. His hospital and private practice developed rapidly, and it was not long before he was recognized as a leading ophthalmologist in Wales. He was a neat and careful operator, who adhered to well-tried and orthodox technique, which his excellent results more than justified. Moreover, he was not only a sound ophthalmologist, but also an experienced Physician, whose belief in his own abilities gave him an assured manner with both patient and doctor. In abstruse or difficult cases, however, he was always ready to call a colleague into consultation. In his earlier days he was frequently seen at clinical meetings as a member of the Ophthalmological Society of the United Kingdom, the South West Ophthalmological Society, and a founder member of the Oxford Congress. He acted for many years on the General Committee of this Journal.

His spare, well-groomed figure and lean features with clipped moustache suggested a military background; never effusive, he had the quiet assured manner of one who, having pondered his problems, came to definite conclusions, and was rarely prevailed upon to alter

them. He always seemed to have his emotions under control, and only a twinkle revealed his sense of humour or a tightening of his jaw muscles his displeasure; he rarely displayed anger in his speech. He enjoyed the company of his friends, whom he chose with care, and he was fond of all sports, but golf, at which he had a single figure handicap, was his favourite form of recreation.

To a large circle of friends, colleagues, and to innumerable patients, his was a personality which will be remembered and mourned. To his widow and family we tender our deepest sympathy.

J.J.H.

CORRESPONDENCE

RECESSION OF THE INFERIOR OBLIQUE

To the Editorial Committee of

THE BRITISH JOURNAL OF OPHTHALMOLOGY

DEAR SIRS,—I have read with interest the article written by Mr. Ivor Lloyd on the subject of recession of the inferior oblique muscle, but I doubt whether the writer's view concerning the cause of overaction of the inferior oblique is as convincing as that of Chavasse. According to Chavasse* the "elevation in adduction" in a case of convergent strabismus free from obvious paresis of the ipsolateral superior oblique, or contralateral superior rectus, is due to the fact that, when an eye is adducted, the inferior oblique's elevating action is intensified because it is a stronger muscle than its direct antagonist —the superior oblique. Chavasse's explanation is more likely than Mr. Lloyd's. The latter argues that an effort of abduction which involves overaction of the inferior oblique is made in order to counteract excessive convergence.

I agree with the writer concerning the need for correcting both the horizontal and the vertical components in squint, but it is open to question whether there is any advantage in performing a recession of the inferior oblique rather than the simpler procedure of myotomy or myectomy.

It would have been more convincing if the case-results had contained not merely the statement that the overaction of the

* CHAVASSE, F. BERNARD (1939).—Worth's Squint, 7th edition, London.

inferior oblique had been corrected, but rather the actual measurements of vertical deviation, both before and after operation—including those made with the eyes in laevo- and dextro-version.

Yours faithfully,

T. KEITH LYLE.

May 12, 1949.

NOTES

Deaths

AS we go to Press we regret to learn of the death of Dr. D. M. Mackay, formerly Ophthalmic Surgeon at Hull Royal Infirmary. Also of Dr. George Mackay, formerly Lecturer on Ophthalmology in Edinburgh University. Obituary notices will appear in our next issue.

* * * *

Ophthalmological Society of Cordoba

THE next General Meeting of the Ophthalmological Society of Córdoba takes place on November 25, next, for the purpose of re-appointing the office-bearers. Those remaining in office are as follows:—

President, Dr. Roberto Obregón Oliva; *Secretary*, Dr. Alberto Urrets Zavalia (hijo); *Treasurer*, Dr. Roque A. Maffrand,

Any correspondence should be addressed to The Secretary, Calle 27 de Abril 255, Córdoba (R. Argentine).

* * * *

AN exhibition for the blind and the partially blind has been arranged in the Science Museum, South Kensington, from June 11 to 21. This exhibition is not open to the general public, but the organisers will be pleased to welcome those who are specially interested in the welfare of the blind.

Papers submitted for publication should be sent to:—
The Secretary of the Editorial Committee,
British Journal of Ophthalmology,
Institute of Ophthalmology, Judd Street, London, W.C.1

Papers should be accompanied by a statement that they have not already been published elsewhere, and that they will not subsequently be offered to another publisher without consent of the B.J.O. Editorial Board.

All papers must be typewritten in double spacing on one side of the paper only, with a blank margin of 1½ inch. The Author's name and address should be plainly indicated. Illustrations should be detachable from the typescript, and numbered in sequence; and the upper edge of each should be marked "TOP" for the printer's guidance. Each illustration should be marked on the back with the author's name. References to the literature should be listed with the authors' names alphabetically arranged, and set out in the Harvard system, *e.g.*, LANGLEY, J. N. (1919). *J. Physiol.*, **53**, 120. Information concerning reprinted copies will be despatched with galley-proofs to the authors of articles accepted for publication.